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 CLAIMS

[Claim(s)]

1. It is a compound containing the liquid carrier ingredient insoluble in water and (b) living body active substance of the non-polymerization nature which has the viscosity of 5,000cP(s) at least in 37-degreeC which is a compound for the emission by which the living body active substance was controlled, and is not purely crystallized under (a) ambient conditions or physiological conditions.
2. Compound according to claim 1 whose liquid carrier ingredient insoluble in water is cane-sugar 2 acetic-acid hexa isobutyric-acid ester.
3. Compound according to claim 2 with which insoluble liquid carrier ingredient exists in water to total weight of compound in about 99.5 % of the weight - about 10% of the weight of amount.
4. Compound according to claim 3 with which insoluble liquid carrier ingredient exists in water to total weight of compound in about 99.5 % of the weight - about 0.20% of the weight of amount.
5. Compound containing the solvent which an insoluble liquid carrier ingredient dissolves in water further according to claim 2.
6. Compound according to claim 5 which is solvent chosen from group which solvent becomes from ethanol, dimethyl sulfoxide, ethyllactate, ethyl acetate, benzyl alcohol, triacetin, N-methyl pyrrolidone, propylene carbonate, and Glico furol.
7. Compound according to claim 5 with which solvent exists to weight of compound in about 10 % of the weight - about 50% of the weight of amount.
8. Compound according to claim 2 with which compound contains additive further.
9. Compound according to claim 8 chosen from group which additive becomes from biodegradability polymer, non-biodegradability polymer, natural oil, synthetic oil, carbohydrate, carbohydrate derivative, mineral salt, and inactive organic compound.
10. The compound according to claim 8 with which an additive exists to the total weight of a compound in about 1 % of the weight - about 20% of the weight of an amount.
11. The compound according to claim 2 chosen from the group which a living body active substance becomes from the small molecule combined with drugs, a peptide, protein, a nucleoprotein, mucoprotein, a lipoprotein, polysaccharide and those derivatives, heparin, synthetic polypeptide, synthetic protein, or protein, a glycoprotein, a steroid, nucleic acids or those fragmentation, a nucleotide, a nucleoside, an oligonucleotide, a gene, a lipid, hormone, and a vitamin.
12. It is the emulsion which is an emulsion for the emission by which the living body active substance was controlled, and is not purely crystallized under (a) ambient conditions or physiological conditions and which contains at least the living body active substance in the carrier based on a liquid carrier ingredient insoluble in the water of the non-polymerization nature which has the viscosity of cP(s), and 5,000(b) water in 37-degreeC.
13. How to be the approach of prescribing the controlled emission compound according to claim 1 for the patient, and include the process which medicates a host with this compound in an emulsion or a solution.
14. How to be the approach of prescribing the controlled emission compound according to claim 1 for

- the patient, and include the process which medicates a host with this compound by injection.
15. How to be the approach of prescribing the controlled emission compound according to claim 1 for the patient, and include the process which medicates a host with this compound with aerosol.
 16. The controlled emission compound according to claim 1 for using for the therapy of an animal.
 17. The controlled emission compound according to claim 1 for using for an agricultural product.
 18. The controlled emission compound according to claim 1 for using for people's therapy.
 19. The controlled emission compound according to claim 1 for using for inhibition of surgical adhesion.
 20. The controlled emission compound according to claim 1 for using for inhibition of surgical adhesion.
 21. The controlled emission compound according to claim 1 for using in a rebirth of an organization for a skeleton, since it is filled up with a gap.
 22. The controlled emission compound according to claim 1 for using in order to prevent the blood supply to a swelling.
 23. The controlled emission compound according to claim 1 for using as tissue adhesives.
 24. The controlled emission compound according to claim 1 for using for recovery of a blemish.
 25. Carrier matter according to claim 1 for using for the therapy of an animal.
 26. Carrier matter according to claim 1 for using for an agricultural product.
 27. Carrier matter according to claim 1 for using for people's therapy.
 28. Carrier matter according to claim 1 for using for inhibition of surgical adhesion.
 29. Carrier matter according to claim 1 for using for inhibition of surgical adhesion.
 30. Carrier matter according to claim 1 for using in a rebirth of an organization for a skeleton, since it is filled up with a gap.
 31. Carrier matter according to claim 1 for using in order to prevent the blood supply to a swelling.
 32. Carrier matter according to claim 1 for using as tissue adhesives.
 33. Carrier matter according to claim 1 for using for recovery of a blemish.
 34. The controlled emission compound of the shape of an emulsion used as a mouth rinse according to claim 1.
 35. The compound according to claim 1 whose living body active substance is heparin.
 36. The compound according to claim 1 whose carrier is disaccharide acetic-acid butylate.
 37. The compound according to claim 1 whose carrier is JISAKKARIDOESUTERU.
 38. The activity matter is a compound according to claim 1 which is first enclosed in a microsphere and joins the carrier matter after that biologically.
 39. The activity matter is the compound according to claim 1 which can form the complexing agent and complex like cyclodextrin biologically.
 40. The activity matter is a compound according to claim 1 which is the gestalt of a prodrug biologically.
 41. The controlled emission compound is a compound according to claim 1 arranged in the gelatine capsule used for internal use.
 42. The controlled emission compound is a compound according to claim 1 enclosed in a microsphere or a microcapsule.
 43. A microsphere is a compound according to claim 1 which is a biodegradability polymer.
 44. The compound according to claim 1 whose polymer is Pori (DL-lactide-KO-glycolide).
 45. The compound according to claim 1 which the controlled emission compound is made to meet with a microcrystal cellulose or an inactive pharmacological excipient like cellulose acetate, and it is optionally processed into the configuration of SUFEA or others, and can be incorporated into a medication gestalt.

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DETAILED DESCRIPTION

[Detailed Description of the Invention]

Controlled delivery system related application with a hyperviscous liquid This invention relates to a hyperviscous liquid compound effective in delivery of the matter and other applications including coating of an organization, and adhesion prevention.

Background of invention Extensive research has been made in the field of the emission system by which the biodegradability for a living body activity compound was controlled. The matrix (base material) of the biodegradability used for drugs delivery is useful. It is because it does not need for them to remove the removal device (drug-depleted device) which used up drugs.

The most general matrix material for drugs delivery is a polymer. After composition and biodegradability of a macromolecule lactic acid are reported by Kulkarni and others in 1996 ("Polylactic acid for surgical implants, "Arch.Surg., and 93-839 page), the field of a biodegradability polymer has progressed quickly. There are the polymer which consists of polyester like a giant-molecule acid anhydride, poly glycolide, and the poly lactide KOGURI corridor, polyamino acid like the poly lysine, and polyethylene oxide as an example of other polymers reported as what is helpful similarly as a matrix material for a delivery device and a copolymer, acrylic end group polyethylene oxide, a polyamide, polyurethane, poly ortho ester, a polyacrylonitrile, poly phosphagen, etc. Please refer to U.S. Pat. No. 4,891,225 given to Langer and the 4,906,474th (macromolecule acid anhydride) number of an United States patent, U.S. Pat. No. 4,767,628 (the poly lactide, the poly lactide KOGURI corridor acid) given to Hutchinson, and U.S. Pat. No. 4,530,840 (the poly lactide, poly glycolide, and copolymer) to Tice and others.

The decomposition ingredient produced biologically is known well and has bridge formation gelatin. The bridge was constructed over hyaluronic acid and it has been used as a decomposition swelling polymer for living body medicine (U.S. Pat. No. 4,957,744 given to Della Valle and others in 1991). "Surface modification of polymeric biomaterials for reduced thrombogenicity." Polym.Mater, Sci, Eng., and 62 731-735 Page.

Furthermore, the hydrogel of biodegradability has been developed for [which was controlled] drugs delivery as a carrier of hormone, an enzyme, an antibiotic, an antineoplastic drug agent, and a biological activity ingredient like a cel suspension (cell suspension). Not only the emission by which the kind to a local organization or local general circulation was controlled but the thing for which the functional property of the kind carried is maintained in time is attained. Cohen Please refer to given U.S. Pat. No. 5,149,543 as an example. By choosing hydrogel macromere (hydrogel macromers) appropriately, the permeability suitable for various applications in an operation, a medical diagnosis, and a therapy, a pore dimension, and the film that has the range of catabolic rate are generable.

Investigation to use a dispersed system current [many] as a carrier of the matter and an especially biological activity compound, or use it is made. materia medica ---like -- it is -- it is -- the dispersed system used for the formulation as cosmetics can be classified as either a suspension or an emulsion. A suspension is defined as a solid particulate ranging from several nm to hundreds of microns in the dimension distributed by the liquefied medium which used the suspending agent. There are a

microsphere, a microcapsule, and NANOSU fair (nanosphere) in a solid particulate. An emulsion is defined as what one liquid is distributing in the liquid of another side, and is stabilized with the interface film which consists of a surfactant and an emulsifier like a lipid. A W / O type emulsion and O / W type emulsion, a compound emulsion (multiple emulsion), a micro emulsion, a micro liquid particle, and liposome are contained in the formulation of an emulsion. As U.S. Pat. No. 4,622,219 and U.S. Pat. No. 4,725,442 which were published by Haynes are defined, a micro liquid particle is an one-sheet film phospholipid vesicle which consists of a spherical lipid layer which has an oil phase inside. Liposome is a phospholipid vesicle prepared by mixing the polar lipid of water-insoluble nature with a water solution. The entropy which is produced by mixing a water-insoluble nature lipid in water and which is not desirable generates very regular deposition of the film which this alignment which consists of phospholipid which has the shut-up water solution closed.

U.S. Pat. No. 4,938,763 given to Dunn and others melts the thermoplastic polymer of the water-insoluble nature which is non-reactivity in a water-soluble solvent with biocompatibility, arranges the liquid inside of the body, and indicates the approach of forming a transplantation explant on that spot by carrying out dissipation of the solvent and generating a solid transplantation explant. This polymer solution may be put into the inside of the body with a syringe. A transplantation explant can take the configuration of a perimeter cavity. In another example, a transplantation explant is formed from the oligomer polymer of a liquid with reactivity, and excluding a solvent, this oligomer polymer is hardened by the position and usually forms a solid-state by addition of a curing catalyst.

In order to use it in the delivery by which the matter was controlled, many ingredients were evaluated, but the need which is toxicity for the delivery by which the matter was controlled of offering an easy system is still left behind rather than low. For example, the above-mentioned delivery system of a polymer and the added macromolecule matrix, a hydrogel, or others is complicated -- it is -- it is -- preparation of the compound which is easy to break is needed. There is the need which it is easily prepared with the matter which should be sent especially, and can be easily prescribed for the patient of offering the delivery system based on a liquid.

Outline of invention So, the purpose of this invention is offering the easy system for sending the matter. Another purpose of this invention is offering the delivery system based on the liquid which it is easily prepared with the matter which should be sent, and can be easily prescribed for the patient.

The further purpose of this invention is offering the approach for controlling and sending the matter in the system which makes an easy liquid a substrate.

The compound used for the emission by which the matter was controlled is offered, and it is this compound (i),

The viscosity in 37-degreeC which is not purely crystallized under ambient conditions or physiological conditions (if it remains as it is) contains at least the matter by which 5,000(ii) delivery should be carried out with the water-insoluble nature hyperviscous liquid carrier ingredient (HVLCM) of the non-polymerization of cP(s).

In one example this HVLCM For example, ethanol, dimethyl sulfoxide, Ethyllactate, ethyl acetate, benzyl alcohol, a triacetin, N-methyl pyrrolidone, propylene carbonate, the Glico furo (glycofuro), For example, Freon like trichlorofluoromethane and fluoro carbon 21, Wood ether, a propane, butane, dimethylformamide, dimethylacetamide, Diethylene carbonate, a butylene glycol, N-(beta hydronalium methyl) RAKUTAMIDO, JIOKORAN (diokolanes) and other amides, ester, It is mixed with the solvent of the water solubility to which viscosity like the ether and alcohol is reduced, or a miscibility, a liquid carrier ingredient (LVLCM) with more low viscosity is formed, and it is mixed with the matter with which it should be sent before a medicine is prescribed for the patient. In a desirable example, this LVLCM has viscosity smaller than 1000cP. At the time of administration, this compound is arranged on the inside of the body or a front face, and this solvent forms from LVLCM dissipation, the transplantation explant which is spread and emits that matter over a predetermined period and which is very much viscous, or a compound on that spot. By choosing a solvent and HVLCM appropriately, the viscosity covering the large range of the compound before administration and after administration can be attained. In a desirable example, HVLCM is the thing of biodegradability.

In one example, the matter mixed with HVLCM is matter [activity / target / which is helpful to human being's therapy, the therapy of an animal, or the agricultural purpose / biology]. In the agricultural field, the compound which contains suitable activity drugs, for example is applicable to the location for controlling weeds (for example, diquat), an insect (for example, methyl parathion), or a noxious insect. In the zootechnics field, this compound can be used for sending a mixed steroid as a growth promotor of livestock, or sending a vaccine (for example, parvovirus vaccine used for the prevention after mating of a pig). in order that this compound can be used for sending [which is crossed to the large range explained more to a detail below] the activity matter biologically or may prevent surgical adhesion in human being -- activity drugs -- or you may use it without activity drugs. Or you may use it for a skeleton (scaffolding) sake as a playback object of a guidance organization like a periodontium at the restoration (void filling) sake of a gap. In other examples, a compound may be injected into the swollen artery and forms the transplantation explant of the hyperviscosity which prevents the blood supply through which it becomes swollen and passes there. the further example -- setting -- this compound -- a suture -- or you may use it without a suture as an organization adhesion agent. Furthermore in another example, a blemish may be used for a compound as a cover blockaded partially.

In in the living body, including a hard organization [like muscles or a soft organization like a fat, and a bone] whose transplantation explant of a compound is, even anywhere, although limitation is not carried out anywhere in in the living body, it can be arranged anywhere in a cavity again including the coecum of a periodontium, opening, a vagina, the rectum, a nasal cavity, a pocket like the periodontal pocket, or an eye.

It contains in arbitration the additive into which the property of a compound is changed as it asks for this compound.

As an example of the suitable additive which is not limited, there are a biodegradability polymer, a non-biodegradability polymer, natural oil or synthetic oil, a carbohydrate or a carbohydrate derivative, mineral salt, BSA (bovine serum albumin), a surfactant, an organic compound like sugar, and organic salt like a sodium citrate. Generally, so that it does not melt into water, namely, if it is oleophilic more, an additive will decrease the emission rate of a base (substrate) more in comparison with the same compound without an additive a certain forge fire. In one example, it is desirable to use the additive which increases the reinforcement of a compound or a property like porosity (porosity). In one example, HVLCM or LVLCM is used without the base which should be sent combining an additive.

in order to make storage, handling, and delivery easy in another example -- one [otherwise,] of the compounds -- or in order to denaturalize the property beyond it, the compound of HVCLM/base is contained in the 2nd carrier ingredient. The example of the 2nd carrier ingredient which is not what is limited is a liquid into which HVLCM does not melt in a solid-state, a gel formulation, and an endermic delivery system (an emulsion is formed). This base should have the high solubility in HVLCM, and the low solubility in the 2nd carrier ingredient.

For example, the emulsion of underwater HVC114 / base can be offered. The useful emulsion which is within the limits of this invention is mouth washing (mouthwash), and bases are the activity drugs for treating ozostomia, stomatitis, or other lips diseases there.

Moreover, in another example, HVLCM is used as a carrier for prescribing a base for the patient locally. For example, this HVLCM promotes the solubility of biological activity drugs, and endermic conveyance. In another example, HVLCM can be used as a carrier for the insecticide containing DEET. In still more nearly another example, HVLCM is used for for example, a louse eliminator or advancing and sending an inhibitor or a compound like a remedy to hair or the scalp.

Easy explanation of a drawing Drawing 1 is the graph of the methylene-blue burst size from SAIB (cane-sugar acetic-acid isobutyric-acid ester) which showed the burst size by time amount progress (time amount) at percent (for 85% of SAIB, and a white square, 90% of SAIB and a upward triangle are [a black dot / 80% of SAIB, and a downward black triangle] 95% of SAIB).

Drawing 2 is the graph of the theophylline burst size from SAIB which showed the burst size (mg/mg) by time amount progress (time amount) (for 2.5% of theophylline, and a upward triangle, 5.0% of theophylline and a black rhombus are [a black dot / 0.5% of theophylline, and a downward triangle /

1.0% of theophylline, and a black square] 10% of theophylline).

Drawing 3 shows the effectiveness of the sucrose by the methylene-blue emission from 90% of SAIB which showed the burst size in the time amount progress by time amount at percent (for 0% of sucrose (90% of SAIB, 10% of ETOH), and a downward triangle, 2.5% of sucrose (90% of SAIB, 7.5% of ETOH) and a black square are [a black dot] 5.0% of sucrose (90% of SAIB, 5% of ETOH)).

Drawing 4 shows the effectiveness of CAB (cellulose acetate butyrate) by the methylene-blue emission from SAIB which showed the burst size by time amount progress (time amount) at percent (for 5% of CAB (40% of SAIB, 55% of ETOH), and a downward black triangle, 10% of CAB (40% of SAIB, 50% of ETOH) and a black square are [a black dot] 15% of CAB (40% of SAIB, 45% of ETOH)).

Drawing 5 is the graph of the burst size of BSA from the paste of BSA (9%)/SAIB in which the burst size (mg) by time amount progress (time amount) was shown at percent.

Drawing 6 is the graph of the burst size of the chlorhexidine from SAIB/ethylactate (EtLac) which showed the burst size by time amount progress (time amount) at percent (for 50/50 of SAIB/EtLac, and a downward white triangle, 70/30 of SAIB/EtLac and a white square are [a white round head] 90/10 of SAIB/EtLac).

Drawing 7 is the graph of the burst size of the chlorhexidine from SAIB/NMP which showed the burst size by time amount progress (time amount) at percent (for 50/50 of SAIB/NMP, and a downward white triangle, 70/30 of SAIB/NMP and a white square are [a white round head] 90/10 of SAIB/NMP).

Drawing 8 is the graph of the burst size of the chlorhexidine from SAIB/propylene carbonate which showed the burst size by time amount progress (time amount) at percent (for 64% of SAIB, and a downward white triangle, 75% of SAIB and a white square are [a white round head] 85% of SAIB).

Drawing 9 is the graph of the burst size of 2.5% of diclofenac from SAIB/triacetin which showed the burst size by time amount progress (time amount) at percent (for 50/50 of SAIB/triacetins, and a downward white triangle, 70/30 of SAIB/triacetins, and a white square are [a white round head] 90/10 of SAIB/triacetins).

drawing 10 is the graph of the burst size of 2.5% of diclofenac from SAIB/ethanol (EtOH) in case there is nothing with the case where there is a sucrose which showed the burst size by time amount progress (time amount) at percent (it SAIB(s) a white square -- 79% of SAIB, and a downward black triangle -- 82% --) For 88% of SAIB, and a black dot, 88% of SAIB, 2.5% of sucrose, and a white round head are [a black square / 90% of SAIB, and a downward white triangle] 80% of SAIB, and 5% of sucrose.

Drawing 11 is the graph of the burst size of 2.5% of diclofenac from SAIB/EtOH which showed the burst size by time amount progress (time amount) at percent in case there is nothing with the case where there are an additive, CAB, and cellulose aceto propionate ("CAP") (for additive nothing and a downward white triangle, those with CAP and a white round head are [a white square] those with CAB).

Drawing 12 is the graph of the burst size of 2.5% of diclofenac from SAIB/dimethyl sulfoxide (DMSO) in which the burst size by time amount progress (time amount) was shown at percent (white round heads are 70/30 of SAIB/DMSO, and downward white triangles are 90/10 of SAIB/DMSO).

Drawing 13 is the graph of the burst size of the flurbiprofen from SAIB/45%EtOH/5%CAP which showed the burst size by time amount progress (time amount) at percent (a white square is 4.99% of flora BIPUROFEN, and a black rhombus is 9.92% of flora BIPUROFEN).

drawing 14 is the graph of the burst size of the naproxen (a free acid or sodium salt) from SAIB / Glicofurol (glycofurol) which showed the burst size by time amount progress (time amount) at percent (a white round head -- 73% of SAIB, and 5.2% of naproxen (free acid) --) A downward white triangle 60% of SAIB, and 3.6% of naproxen (free acid), A white square 52% of SAIB, and 4.1% of naproxen (free acid), For 74% of SAIB, 5.2% of naproxen (sodium salt), and a downward black triangle, 60% of SAIB, 3.4% of naproxen (sodium salt), and a black square are [a black dot] 52% of SAIB, and 3.9% of naproxen (sodium salt).

Drawing 15 is the graph of the burst size of 2.5% of theophylline from SAIB(40%)/EtOH/CAB which showed the burst size by time amount progress (time amount) at percent, or CAP (for 5% of CAP, and a white square, 10% of CAP and a black square are [a black dot / 5% of CAB, and a black dot / 10% of

CAB, and a downward white triangle / 15% of CAB, and a downward black triangle] 15% of CAP). Drawing 16 is the graph of the burst size of the theophylline from SAIB/propylene carbonate which showed the burst size by time amount progress (time amount) at percent (for 64% of SAIB, and a black dot, 74% of SAIB and a white round head are [a downward white triangle] 84% of SAIB).

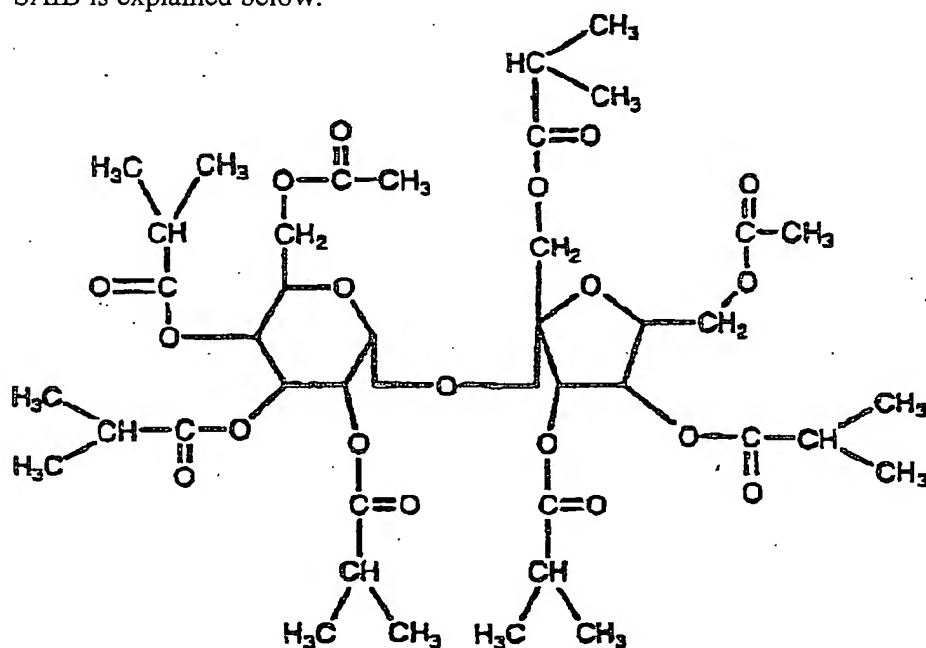
Drawing 17 is the graph of the burst size of two formulations. One preparation (part of a black shadow) The remaining part is diH₂O including **, 3.2% of SAIB, 15.1% of ETOH, and 0.00395% of methylene blue. Another preparation (shadow area)

The remaining part was diH₂O including **, 0% of SAIB, 28.9% of ETOH, and 0.00395% of methylene blue.

Selection of the detailed explanation I. hyperviscous liquid carrier ingredient of a desirable example The hyperviscous liquid carrier ingredient should be chosen, and it is a non-polymerization, and is nonaqueous solubility, and has the viscosity of 5,000cP(s) at least in 37-degreeC (and it has even 10,000, 15,000, 20,000, 25,000, or 50,000cP(s) at least optionally), and it does not crystallize it purely under ambient conditions or physiological conditions (if it remains as it is). Vocabulary called water-insoluble nature means the ingredient with which only extent fewer than 1 % of the weight can melt into water under ambient conditions.

In a desirable example, HVLCM forms LVLCM mixable with the base which viscosity decreases considerably and is used for the controlled delivery, when it mixes with a solvent. Generally, the compound of LVLCM/base is easier to arrange inside of the body than the compound of HVLCM/base. It is because the compound of LVLCM/base flows easily by the inside and outside of transfer pipet or other impregnation means and it can prepare easily as an emulsion. LVLCM can have all desired viscosity. The application in the living body understands more that the viscosity field of LVLCM smaller than about 1000 cP(s) and the viscosity field smaller than 200cP in a detail are usually useful. In one example, HVLCM is disaccharide ester like disaccharide 2 acetic-acid hexa butylate.

In a desirable example ("SAIB"), i.e., cane-sugar acetic-acid isobutyric-acid ester, the sucrose molecule which two acetic-acid parts and six isobutyric-acid parts esterified is used as HVLCM. The structure of SAIB is explained below.



SAIB is nonpoisonous in taking orally and is used as what stabilizes an emulsion in current and the food industry. It is a liquid which has viscosity very much, and has the peculiar property in which viscosity changes with slight heating or addition of a solvent dramatically. It is fusibility to many biocompatibility solvents. SAIB may be applied by impregnation or aerosol spraying when it is in the dissolved condition

or the condition of an emulsion. SAIB has the cellulose ester which can affect the rate which sends the matter, and other polymers and compatibility.

In another example HVLCM Propylene glycol, glyceryl, A diethylaminoethyl and stearate ester like it of a glycol, N and N'-ethylene JISUTE aramid and steer RAMIDO MEA -- and The stearate amide and the other long-chain-fatty-acid amides like steer RAMIDO DEA, Ethylene BISUTE aramid (ethylene bistearamide), Cocoamine oxide (cocoamine oxide), cetyl alcohol, and long-chain fatty alcohol like stearyl alcohol, You may be long-chain ester like Millis Chill Millis Tait, BEHENIERUKETO (beheny erucate), and glyceryl phosphate. In a specific example, HVLCM is acetylated sucrose distearate (Crodesta A-10).

HVLCM may be contained in a compound in any amount which realizes a desired operation. For example, HVLCM may be used as organization coating with the base which may use it independently as a protective coat or a bolus (bolus), or increases the property or effectiveness of an ingredient for adhesion prevention. HVLCM is contained in the controlled delivery compound in the amount in about 99.5 % of the weight - about 0.20% of the weight of the range. Generally it is contained in the controlled delivery compound in the amount in about 99.5 % of the weight - about 10% of the weight of the range, and HVLCM is 95 - 25 % of the weight to the AUW of a compound, and, most generally is 85 - 45 % of the weight.

Matter which should be II(ed) . sent If this approach is used, any matter which presents a desired property can be sent. Preferably, the matter is activity matter biologically.

The vocabulary "matter [activity / target / biology]" which is used here drugs, a peptide, protein, and a carbohydrate (monosaccharide and oligosaccharide -- and) The nucleoprotein and mucoprotein containing polysaccharide, a lipoprotein, synthetic polypeptide, or synthetic protein, Or the small molecule combined with protein, a glycoprotein, a steroid, A nucleic acid (all gestalten of DNA including CDNA, RNA, or those fragmentation), A nucleotide, a nucleoside, an oligonucleotide (an antisense oligonucleotide is included), An organic molecule including the vitamins containing a gene, a lipid, hormone, vitamin C, and vitamin E or those combination is meant. These organic molecules Biological effectiveness is brought about when the inside of the body of the animal which is not limited to it is medicated, although a bird and mammals including human being are included.

Vocabulary called drugs which are used here Treatment, a therapy, Or all the matter used externally as a chemical used for prevention of a disease or abnormalities or inner is meant. An immunosuppressant, an antioxidant, an anesthetic, a chemotherapeutic drug (chemotherapeutic agent), A steroid (a retinoid is included), hormone, an antibiotic, an antiviral drug, An antifungal drug, anti-breeder material, an antihistamine, an anticoagulant, an anti-light aging agent (antiphotaging agent), An intermedin peptide (melanotropic peptide), Limitation is not carried out although a non-steroid anti-inflammation compound and a steroid anti-inflammation compound, an antipsychotic drug, and a radiation absorbent (radiation absorber) including UV absorbent are included.

Vocabulary called the activity matter also contains an insecticide, a damage-by-blight-and-harmful-insects prevention agent, a germicide, a rodenticide, a vegetable nutrient, and drugs like a plant growth promoter biologically again.

In one example, a compound is a vaccine and the matter which should be sent is an antigen. This antigen is obtained from a cell, bacteria, virions, or those parts. Antigens may be protein, a peptide, polysaccharide, a glycoprotein, a glycolipid, nucleic acids, or those combination, and it pulls out the immunoreaction in mammalian, a bird, or an animal like a fish so that it may define here. An immunoreaction may intervene body fluid or a cell so that it may define here. When the ingredient to which an immunoreaction should be turned is lacking in antigenic, it may be joined to the carrier or hapten like albumin using one of the reagent kits with which some are marketed, using a standard covalent-bond technique.

As an example of a desirable antigen, there are influenza protein, human immunodeficiency virus protein and A mold, B mold or the protein of a virus like hepatitis C protein, protein of bacteria, a cell wall of a gram negative, Neisseria gonorrhea protein, and lipopolysaccharide like a parvovirus.

As an example which is not what a materia medica-ingredient limits Nitrofurazone and an antiinfective

drug like sodium propionate, Penicillin, a tetracycline, oxytetracycline, chlorotetracycline, Bacitracin, a nystatin, streptomycin, a neomycin, a polymyxin, gramicidin, a chloramphenicol, and an erythromycin - and An antibiotic including azithromycin (azithromycin), Sulfacetamide, sulfamethizole, the sulfamethazine, sulfadiazine, A sulfamerazine and the sulfonamide containing sulfisoxazole, And the antiviral drug containing idoxuridine, antazoline, methapyrilene, Chloro pheniramine, mepyramine, pro FEMPIRIDAMIN (prophenpyridamine), Hydrocortisone, cortisone, hydrocortisone acetate, dexamethasone, Dexamethasone 21-phosphoric ester, fluocinolone, triamcinolone, The medrysone, prednisolone, and prednisolone 21-sodium succinate, And an antiallergic agent like prednisolone acetate, a ragweed pollen antigen, A desensitizer like the hay fever pollen antigen, a dust antigen, and a cow's milk antigen (desensitizing agent), Variola, yellow fever, distemper, hog cholera, chicken pox, anti BENOMU (antivenom), Scarlet fever, diphtheria (dyptheria), toxoid, tetanus toxoid, ****, pertussis, influenza rabies, mumps, measles, poliomyelitis anterior acuta, And the vaccine for the New Castle disease, phenylephrine, naphazoline, And an antiphlogistic like tetrahydrozoline, pilocarpine, ESUPE phosphorus salicylate (esperine salicylate), Carbachol, a diisopropyl phosphofluoridate salt, iodation phospholine (phospholine iodide), And the miosis agent and anticholinesterase like a demecarium bromide, Atropine sulfate, cyclopentolate, homatropine, scopolamine, Tropicamide, eucatropine, and a parasympathetic nerve Mr. agent like hydroxyamphetamine, A sympathetic nerve Mr. agent like epinephrine, pentobarbital sodium, Phenobarbital, secobarbital sodium, codeine, a urea (alpha-BUROMO iso valeryl), A sedative and hypnotic like cull BUROMARU, 3-(2-aminopropyl) Indore acetate, And a psychic energizer like 3-(2-amino butyl) Indore acetate, Reserpine, KURORU pro my phosphorus (chlorpromayline), And a tranquilizer like thiopropazate, methylthioadenosine, And a male sex hormone steroid like a full ORIME sterone (fluormesterone), Estrone, 17-beta-estradiol, ethinylestradiol, And estrogen like a diethylstilbestrol, progesterone, Non [megestrol (megestrol), meringue SUTORORU, and clo serious] The ethisterone, the norethynodrel, 19-norprogesterone, the norethindrone, An ovulation inducing drug like medroxyprogesterone and 17-beta-hydroxyprogesterone, PGE1, PGE2, and PGE3 etc. -- PUROSUTAGURAJIN and an antipyretic like aspirin -- [for example,] Sodium salicylate and a body fluid agent like salicylamide (humoral agent), Atropine, methantheline, papaverine, and an anti-convulsive agent like the methscoplamine bromide, 4-amino quinoline, 8-amino quinoline, chloroquine, and antimalarial like the pyrimethamine, Diphenhydramine, the dimenthhydrinate, tripelenamine, the perphenazine, And an antihistamine like KURORU phenazine (chlorphenazine), Dibenzo hydronalium full MECHIAZAIDO (dibenzhydroflume thiazide), The flumethiazide, the chlorothiazide, and a heart agent like amino TORETO (aminotrate), There are a growth factor, a cell adhesion factor, cytokine and a vitamin including a biological reaction modifier (response modifier), nature, a composite bioactive peptide, and a nutrient like protein.

Sufficient amount for an activity compound to send the effective dose for attaining desired effectiveness to the animal or vegetation which is a host is contained in a compound. It depends for the amount of the drugs, i.e., biological activity drugs, contained in a compound on the concentration of the drugs needed for the emission characteristic for which it asks, and biological effectiveness, and the emission period of desired drugs.

Furthermore, it depends for the concentration of the activity compound in a compound also on the other factors known by this contractor again depending on the absorbed amount, the amount of inactivation, and the amount of elimination of drugs. Moreover, it will turn out that it changes by severe [in the condition that a dose should also be mitigated]. Also as opposed to subject like an individual throat furthermore, a specific medication plan He should understand that it must be adjusted according to special decision of those who continue for the whole period, and manage or superintend each initial complement and administration of a compound. Moreover, the density range described here is only merely described as an example, and should understand that it is not what is going to limit the range of a compound or operation indicated by the claim. A compound may be prescribed for the patient with 1 time of a dose, or may be divided into the dose of some small amounts, and may be prescribed for the patient in various time intervals.

a biological active substance is contained in a compound in about 0.5 % of the weight - about 20% of

the weight of the range to the AUW of a compound, and, more typically, there are than about 1 Wt(%) of the weight and the following -- the same) % - about 15 Wt(s)% or it. [more] Another desirable range is about 2 Wt(s)% - about 10 Wt(s)%. About very activity drugs like a growth factor, the desirable range is less than [1 Wt%], therefore it is 0.0001% or less.

Both the fusibility matter and the insoluble matter may be dissolved in HVLCM or LVLCM used for the controlled delivery.

III. additive In order to change the property of an ingredient into a desired property, various additives may be added by HVLCM or LVLCM as optional. An additive can be contained in the amount of sufficient arbitration to give a desired property to a compound. Generally, the amount of the additive used is the function of the property of an additive, and the effectiveness which should be attained, and an activity person in charge can determine it easily.

When contained, an additive is typically contained in a compound in the amount which is in the range of about 0.1 Wt(s)% - about 20 Wt(s)% to the AUW of a compound, and, more typically, is contained in a compound 1 Wt% in the amount in the range from 2 Wt% or 5 Wt% to about 10 Wt(s)%. An additive of a certain kind like a buffer is only contained in a compound in few amount.

The following classifications are the examples of the class which is not what the additive which can be used in a compound limits. If an indication here and the purpose which it is going to attain are given, the person well versed in this field can know easily how various additives will be chosen, in order to attain the desired purpose. It is considered that all these examples are in the range of indicated this invention.

A. Biodegradability polymer One classification of an additive is the polymer and oligomer of biodegradability. A polymer can be used in order to change the emission characteristic of the matter which should be sent and to give a binding property (integrity) to a compound, otherwise in order to change the property of a compound. As an example which is not what the polymer of suitable biodegradability and oligomer limit Pori (lactide), Pori (lactide-KOGURI corridor), Pori (glycolide), Pori (caprolactone), a polyamide, the Pori anhydride (polyanhydride), Polyamino acid, poly ortho ester, poly cyanoacrylate, Pori (phospha gin), Non [Pori (phospho ester), polyester amide, and poly diox] Polyacetal, the poly ketal, a polycarbonate, poly alt.carbonate, Resolvability polyurethane, poly hydronalium KISHIBUCHIETO (polyhydroxybutyi-ate), The combination or mixture which consists of those copolymers, a terpolymer, an oxycellulose, or an above-mentioned ingredient is in polyhydroxyvalerate, a polyalkylene OKISA rate, polyalkylene succinate, Pori (malic acid), a chitin, chitosan, and a list.

As an example of Pori (a-hydroxy acid), Pori (glycolic acid), Pori (DL-lactic acid), Pori (L-lactic acid), and these copolymers exist. As an example of poly lactone, there are Pori (e-caprolactone), Pori (d-valerolactone), and Pori (gamma-butyrolactone).

B. Non-biodegradability polymer The further additive used with the compound by this invention is a non-biodegradability polymer. As an example which is not what the non-biodegradability polymer which can be used as an additive limits, there are polyacrylate, an ethylene vinyl acetate polymer, a cellulose and a cellulosic, an acylation cellulose and its derivative, non-corrosive polyurethane, polystyrene, polyvinyl chloride, a polyvinyl fluoride, polyvinyl imidazole, chloro sulfonation polyolefine, and polyethylene oxide.

As a desirable non-biodegradability polymer, there are polyethylene, a polyvinyl pyrrolidone, ethylene vinyl acetate, a polyethylene glycol, a cellulose acetate butyrate ("CABO"), and acetic-acid cellulose propionate ("CAP").

C. An oil and fat The further class of additive which can be used in the compound by this invention is the oil and fat of nature and composition. Generally there is a glyceride of the fatty acid which mainly consists of oleic acid, a palmitic acid, stearin acid, linolic acid, etc. from an animal as an oil obtained from the kind of a vegetable fruit. Generally, as for an oil, viscosity increases more, so that a molecule contains more hydrogen.

As an example which is not what suitable natural oil and synthetic oil limit, a middle chain fatty-acid triglyceride is in nature or the refined vegetable oil, peanut oil, a middle chain triglyceride, soybean oil, an almond oil, olive oil, sesame oil, peanut oil, fennel oil, camellia oil, corn oil, castor oil, cotton seed

oil and soybean oil, and a list.

Typically, a fat is glyceryl ester like stearin acid and a palmitic acid which consists of a higher fatty acid more. At a room temperature, such ester and mixture of that are a solid-state, and present crystalline structure. Lard and beef tallow are the example. Generally, an oil and fat increase the hydrophobicity of SAIB and delay decomposition and water absorption.

D. A carbohydrate and carbohydrate derivative Another class of additive which can be used in the compound by this invention is a carbohydrate and a carbohydrate derivative. As an example which is not what these compounds limit, there are monosaccharide (fruit sugar and simple sugar like the isomer glucose (grape sugar) of that), cane sugar, a maltose, a cellobiose, disaccharide like a lactose, and polysaccharide.

IV. solvent When a compound is used as LVLCM, it must contain a solvent with meltable HVLCM. Preferably, the matter which should be sent is also meltable to a solvent. A solvent must be nonpoisonous, and must have water solubility or water compatibility, otherwise must have biocompatibility. A toxic solvent should not be used for the pharmacological or agricultural purpose. the organization in an impregnation location if the solvent used for pouring a compound into an animal is not the effectiveness of asking for a stimulus or a necrosis -- ***** -- a stimulus or a necrosis should not be made to cause

A solvent must be water solubility at least and a solvent can be quickly diffused by it by the environment containing the water of the body fluid or others which makes a compound solidify or solidify. As an example of a suitable solvent, there are ethanol, ethyllactate, propylene carbonate, the Glico furol (glycofurol), N-methyl pyrrolidone, 2-pyrrolidone, propylene glycol, an acetone, methyl acetate, ethyl acetate, a methyl ethyl ketone, benzyl alcohol, a triacetin, dimethylformamide, dimethyl sulfoxide, a tetrahydrofuran, a caprolactam, DESHIRU methyl sulfoxide, oleic acid, and 1-dodecylazacycloheptane-2-one.

When SAIB is used as HVLCM, desirable solvents are ethanol, dimethyl sulfoxide, ethyllactate, ethyl acetate, benzyl alcohol, a triacetin, N-methyl pyrrolidone, propylene carbonate, and the Glico furol. SAIB does not have compatibility with glycerol, corn oil, peanut oil, 1, 2-propanediol, a polyethylene glycol (PEG200), super-purification sesame oil, and super-purification peanut oil. Therefore, the latter group's solvent of using it with SAIB is not desirable.

Typically, a solvent is added by the compound in the amount which is in the range of about 5 Wt(s)% - about 55 Wt(s)% to the AUW of a compound. Preferably, a solvent is contained in a compound in the amount in the range of about 10 Wt(s)% - about 50 Wt(s)%. Another desirable range is about 10 Wt(s)% - 30Wt%.

V. Use of a LVLCX compound and a HVLCX compound A host can be medicated with the compound described here by various approaches which may differ according to the result which should be attained. When a host is an animal like human being, a compound may be locally prescribed for the patient systematically (for example, in membrane (based on a nasal cavity according to the vagina by the rectum by taking orally), or parenterally (it depends in the peritoneum according to the intramuscular by hypodermically by the vein)), using a suitable carrier, if wanted. When a compound is used for the agriculture-purpose, it may be applied using the equipment for impregnation, spraying immersion (sprays dip), aerosol, or spreading.

Drugs or animals are preferably medicated with the compound by this invention by the paste as a solution by impregnation or aerosol, or the emulsion. When a medicine is prescribed for the patient by impregnation as LVLCM, the solvent of the small amount used for a compound permeates the aqueous fluid of a host, and forms coating for the storage area (depot) of the hyperviscosity used for the delivery by which the matter was controlled, or the organization which can make adhesion prevention or the minimum. When used by aerosol or the emulsion, the solvent of few amounts in a solution evaporates in administration and coincidence, and LVLCM makes it possible to act as HVLCM. Generation of aerosol and an emulsion is realizable using the technique well known to the person well versed in this field. For example, please refer to Ansel, Pharmaceutical Dosage Forms and Drug Del'Systems by H.C. and others, sixth ed., and 1995.

A compound can be used for forming protection organization coating, and can be used for preventing formation of surgical adhesion especially. Since HVLCM can adhere to a perimeter organization or a bone, it can be poured into hypodermically like a collagen for formation of an organization, or restoration of a deficit. Furthermore, HVLCM may be poured into damage including a burn blemish in order to prevent that a deep scar is formed. The resolving time of HVLCM can be adjusted by using a polymer as an additive to HVLCM. Therefore, the transplantation explant formed of HVLCM enables a transplantation explant to disappear while biodegrading slowly in a body, a natural organization's growing and it replacing a transplantation explant.

In another example, biologically, at first, the activity matter may be enclosed in the microsphere and built into the carrier ingredient of this invention after that.

In another example, the activity matter can form the complexing agent and complex like cyclodextrin biologically. Furthermore in another example, the activity matter is the gestalt of a prodrug biologically. As a means of others for using this invention The formulation for a carrier or the controlled emission is arranged in the gelatine capsule used for internal use. The formulation for a carrier or the controlled emission is enclosed in a microsphere or a microcapsule. Preferably A microsphere is a biodegradability polymer like Pori (DL-lactide-KOGURI corridor). The formulation for a carrier or the controlled emission is made to meet with a microcrystal cellulose or an inactive pharmacological excipient like cellulose acetate. And it There is a means [like] which it is processed into the configuration of SUFEA or others, and can be incorporated into a medication gestalt as an option.

[A local oral cavity delivery compound]

According to this invention, the local oral cavity delivery compound which consists of HVLCM which are a surfactant, an auxiliary surfactant (cosurfactant), and an oily component, for example, cane-sugar acetic-acid isobutyric-acid ester, and water which can maintain delivery of the activity drugs to the oral cavity can be prepared.

This invention may be used for preparing the gargle which acts over the long duration containing SAIB and the activity drugs by the 2nd water carrier ingredient in the gestalt of an emulsion. If it is used by the general approach before a gargle lies down, ozostomia will decrease at the next morning, for example.

The component in the formulation of a gargle can be classified into an antimicrobial agent, a surfactant, an auxiliary surfactant, an oily component, cane-sugar acetic-acid isobutyric-acid ester, water, and six groups that consist of additives. Each of these groups is explained to a detail below. If there is this specification, the person familiar with this field can prepare the local oral cavity delivery system of others which are used for the application covering stomatitis and the large range including the therapy used for other diseases of oral cavity by choosing suitable activity drugs.

[Antimicrobial agent]

Although limitation is not carried out to the antimicrobial activity drugs used in the formulation of a gargle today, there are domiphen bromide, triclosan (triclosan), chlorhexidine, essential oil, cetylpyridinium chloride, a fluoride, alexidine (alexidine), salicylanilide, a zinc compound, and an antibiotic. or [that these are used independently] -- or it may be combined and used and the combination of cetylpyridinium chloride and a zinc compound division zinc gluconic acid (zinc gluconate) is desirable.

[Surfactant]

Although the surfactant chosen has water solubility, and it is a nonionic thing and limitation generally is not carried out in order to use it in the formulation by this invention, there are independent or the polyoxyethylene castor oil combined and used, polyoxyethylene hydrogenation castor oil, polyoxyethylene sorbitan fatty acid ester, polyoxyethylene alkyl ester, polyoxyethylene alkyl ether, polyoxyethylene glycerol ester, a sorbitan fatty acid ester, etc. There are polyoxyethylene sorbitan fatty acid ester which has 5-40-mol ethylene oxide, and polyoxyethylene glycerol ester which has 5-20-mol ethylene oxide in a desirable nonionic surface active agent. Polyoxyethylene (20E.O.) sorbitan monooleate, a polyoxyethylene (20E.O.) almond oil, polyoxyethylene (20E.O.) hydrogenation castor oil, or a thing similar to it is desirable especially.

The amount of the surfactant by which homogeneity mixing should be carried out changes with the classes of surfactant used to the formulation by this invention. Generally, the desirable range is 1 - 60Wt%, and especially the desirable range is 2 - 10Wt%.

[Auxiliary surfactant]

Generally, the auxiliary surfactant used in the formulation by this invention means the nonionic component which has low low hydrophilicity / oleophilic ratio (HLB) of alcohol, or a surfactant / auxiliary surfactant system. In the formulation by this invention, the auxiliary surfactant which has a function as a solubilizing agent or an auxiliary solvent, and also has a function as a surfactant further is desirable. As such an auxiliary surfactant, monohydric alcohol, polyhydric alcohol, or the nonionic surfactant of low HLB may be used in either independent or the combination beyond those two or them. As an example of monohydric alcohol, there are benzyl alcohol, ethyl alcohol, octyl alcohol, and a thing similar to them, and there are propylene glycol, a glycerol, 1, 3-butylene glycol, and a thing similar to them as an example of polyhydric alcohol. As an example of the nonionic surfactant of low HLB, the polyethylene glycol of 300-4,000 has the distilled monoglyceride, poly glycerol poly oleate, and molecular weight. The more desirable example of an auxiliary surfactant is poly glycerol poly oleate. Especially a desirable auxiliary surface active agent is decaglyceryl tetra-oleate.

The amount of these auxiliary surfactants by which homogeneity mixing should be carried out changes with the classes of auxiliary surfactant used to the formulation by this invention. Generally, the desirable range is 0.5 - 30Wt%, and especially the desirable range is 1 - 5Wt%.

[An oily component]

One or the oily component beyond it typically chosen from a glycerine fatty acid ester, fatty acid ester, fatty alcohol and those derivatives, fatty alcohol benzoate, and the group that consists of a hydrocarbon may be used as an oily component in the formulation by this invention. Although they will be obtained from a natural resource, although it is a synthetic compound, or although an acceptable monoglyceride, diglyceride, triglycerides, or those mixture are semisynthesis compounds, they may be used for those sources or origins as a glycerine fatty acid ester without relation. A desirable glycerine fatty acid ester has the nature of an almond oil, olive oil, sesame oil, peanut oil, fennel oil, camellia oil, corn oil, castor oil, cotton seed oil, and soybean oil or the refined thing, middle chain fatty-acid triglycerides and independent [these], or the combined thing. Especially a desirable thing is a middle chain fatty-acid triglyceride.

Desirable fatty acid ester is the isopropyl myristate, octyl palmitate, ECHIRUORIETO, and ethyl palmitate. Especially desirable things are the isopropyl myristate and octyl palmitate. Especially desirable fatty alcohol derivatives and fatty alcohol benzoate are 2-octyl dodecanol and C12-15 alcoholic benzoate. A light or heavy liquid paraffin oil is the example of a desirable hydrocarbon. These oily components are independent or may be used combining other oily components. Homogeneity mixing can be carried out in a 0.5 - 50Wt% amount at the formulation by this invention, and these oily components are 1 - 10Wt% preferably.

[Cane-sugar acetic-acid isobutyric-acid ester]

The cane-sugar acetic-acid isobutyric-acid ester explained to the detail in the top is used as HVLCM. Typically, homogeneity mixing is carried out in a 0.01 - 10Wt% amount at a formulation, and SAIB is 0.1 - 2Wt% preferably.

[Water]

Another essential component contained in the formulation of a gargle is water. It is pH3-pH10, and the formulations by this invention are pH5-pH9, and are pH6-pH8 more preferably. A buffer may be used in order to maintain a pH value in the above-mentioned range. As an example of a desirable buffer, an acetic acid, citric acid, phosphoric acid, benzoic acids, and/or those salts exist. A pH value may be preferably adjusted to the desirable range according to the adjustment demanded an acid or a base suitable at the time of manufacture, and by adding a hydrochloric acid or a sodium hydroxide. Furthermore, as for the water used in the formulation of this invention, being deionized and filtered is desirable.

[Additive]

Although it is similar to antiseptics, a stabilizer, an antioxidant, a coloring agent, an isotonicity agent (isotonic agent), a seasoning, a moisturizer, a sequestering agent, a vitamin, a vitamin precursor, and them, the component of others [like] may be added if needed. As a desirable example of antiseptics, there is a paraben derivative (paraben derivative) and there are methylparaben and propylparaben as most desirable antiseptics. As a desirable example of an anti-oxidant, there are butylhydroxyanisole, butylhydroxytoluene, propyl gallate, vitamin-E acetate, and a purification hydroquinone, and the most desirable anti-oxidants are vitamin-E acetate and butylhydroxytoluene. There is a sorbitol as a desirable example of a moisturizer. As a desirable example of a seasoning, there are a pepper oil, spearmint oil, wintergreen oil, menthol, and saccharin. There is citric acid as a desirable example of a sequestering agent.

A local oral cavity delivery system may be prepared by mixing two phases under the temperature which blends the phase of an oil, and the phase of water separately, and rises by the conventional approach. In advance of PAKKESHINGU, it is fully mixed and the mixture of the phase of this oil and the phase of water is awake to a room temperature.

VI. example By this indication, this contractor can prepare and use various HVLCH compounds covering the large range. Probably, all these examples are included in the range of this invention. In order to make it more intelligible, the following examples explain preparation and use of a SAIB compound to a detail. other HVLCM(s), an additive, a base, and a solvent are the same -- it is -- it is -- it may be used by the similar approach.

In order to prepare a desired formulation, the following general procedures were used in the example. in order to melt the activity matter biologically in SAIB / solvent system, do preparation in the scintillation vial of 20mL -- and a swing and stirring -- and/or, it heated. In the example into which the activity matter did not melt biologically, in order [in a liquid particle condition] to acquire the best distribution of the activity matter biologically, the formulation was cooled and stirred.

Emission out of the living body of an activity compound was biologically checked using the following general procedures. pH7.4 -- or the phosphoric-acid buffer solution ("PBS") (10mL) of pH6.8 was added in the 16x125mm test tube. The pH value of this pH7.4 or pH6.8 was biologically chosen based on the application and solubility of the activity matter. In order to prevent growth of a microorganism, PBS was a thing containing 0.2% of sodium azide. The formulation of the matter [activity / target / 0.03-0.09g / SAIB / solvent / biology target] was extruded to disposable plastics pipet blank test tubing, and the weight was recorded. The test tube covered and put it on the shaker bus (shaker bath) which is set as 37-degreeC and swayed continually.

The test tube was periodically picked out from the shaker bus at some times. It put into the test tube which took out PBS from the test tube containing a formulation, washed it, and was then dried. In an PBS solution in order to judge the amount of an activity ingredient biologically, UV analysis of these samples was carried out. New PBS was put into the test tube containing a formulation, and the test tube was returned to the shaker bus. This procedure was repeated at the time of some from which a sample is obtained.

The concentration of an activity ingredient was biologically used [which creates an emission profile based on the original amount of an activity ingredient biologically] also in the formulation in the emission solution. This amount was judged using ultraviolet visible spectrophotometry.

At these examples, they are ethanol (EtOH), dimethyl sulfoxide (DMSO), ethyllactate (EtLac), ethyl acetate (EtOAc), benzyl alcohol (FCH₂OH), a triacetin, N-methyl pyrrolidone (NMP), propylene carbonate (PC), and the Glico furol (GF).

eye **** -- various solvents were used.

Generally the bigger rate (%) than that of a solvent brought the biology target in a formulation bigger concentration than that of the activity matter. Moreover, the amount and class of solvent were also directly related to the viscosity of a solution. Table 1 makes a table effect of the solvent about the mixture of SAIB/solvent, and concentration. This viscosity data was obtained by 30-degreeC using the Cannon-Fenske viscometer of 200 molds.

| 表 1 | |
|-----------------------|-------------|
| 材料 | センチボイズ (cP) |
| rodH ₂ O | 1 . 0 |
| EtOH | 1 . 3 |
| 60/40 SAIB/EtOH | 7 . 7 |
| 70/30 SAIB/EtOH | 17 . 0 |
| 55/40/5 SAIB/EtOH/CAB | 68 . 9 |
| 90/10 SAIB/EtOH | 494 . 8 |
| PC | 2 . 1 |
| 70/30 SAIB/PC | 138 . 7 |
| 70/30 SAIB/グリセロール | 228 . 4 |
| ピーナッツ油 | 57 . 8 |

It is the effectiveness of the activity matter biologically. In order to prove drugs emission, a methylene blue and cow serum albumin (BSA) were used. Chlorhexidine, diclofenac, the doxycycline, flurbiprofen, naproxen, and theophylline were contained in the component [activity / target / which is emitted from a system / biology]. Emission was not maintained for the low dissolved water in fuel of clotrimazole.

Example 1 Ethanol (1g) was mixed with cane-sugar acetic-acid isobutyric-acid ester (SAIB) (9g). After mixing calmly, the solution of transparent low viscosity was obtained. The drop of this solution was emitted into water from the glass pipet, the spherical matrix was formed, and this matrix maintained that configuration one week or more.

Example 2 Ethanol (2g) was mixed with SAIB (8g). The obtained solution formed the thin film, when it mixed with water. This film maintained that configuration one week or more.

Example 3 According to the procedure of an example 1, ethanol and the amount of SAIB were changed and the solution was prepared. 0.07% of methylene blue was added in this solution. As the example 1 explained, the spherical drop was formed in phosphoric-acid buffer solution (PBS). The PBS sample was maintained to 37-degreeC. PBS was taken out periodically and analyzed the content of a methylene blue by ultraviolet visible spectrophotometry. The result of the burst size of a methylene blue is shown in drawing 1.

Example 4 Cow serum albumin (BSA) was used instead of the methylene blue, and a series of formulations were prepared according to the procedure of an example 3. In these formulations, BSA, a solvent, and various rates of SAIB were used. The class of solvent and BSA, a solvent, SAIB, and the ratio of all additives are indicated to the following tables 2-4. Emission of BSA was delayed by making the ratio of CAP:SAIB increase:

In this system, BSA was insolubility. Although it was going to solubilize it using the partially aromatic solvent, BSA was fusibility only in the glycerol and water whose SAIB is not compatibility. In the emission characteristic, all the formulations contained in BSA were heterogeneous. Table 2 is a chart of the formulation containing BSA.

表 2

| % B S A | % EtOH | % P V P | % 5 0 / 5 0 グリセロール/DMSO |
|---------|--------|---------|----------------------------|
| 2 7 | 3 7 | 0 | 4 . 4 |
| 4 . 6 | 3 6 | 0 | 5 . 6 |
| 5 . 5 | 3 6 | 0 | 5 . 8 |
| 5 . 0 | 3 3 | 5 . 9 | 6 . 9 |
| 5 . 5 | 3 1 | 8 . 2 | 8 . 3 |
| 4 . 9 | 2 7 | 1 8 . 8 | 9 . 8 |

表 3

| %BSA | 溶剤 | %溶剤 | 添加剤 | %添加剤 |
|-------|-------------------------|---------|----------------------|-------|
| 1 . 1 | P C | 3 1 . 3 | d i H ₂ O | 9 . 8 |
| 9 . 2 | 溶剤は使用せず (BSA/SAIBのペースト) | | | |
| 9 . 6 | グリセロール | 9 . 2 | — | — |
| 1 . 9 | EtOH | 3 0 | — | — |
| 1 . 9 | EtOH | 2 0 | — | — |
| 1 . 9 | EtOH | 1 0 | — | — |
| 1 0 | EtOH | 1 0 | — | — |

Drawing 5 shows the emission characteristic about the paste of SAIB/BSA formed without using an additional solvent at all.

Although it tried to acquire the emission characteristic, it was not obtained from the heterogeneous formulation shown in Table 4.

表 4

| %BSA | 溶剤 | 溶剤% | 添加剤 | 添加剤% |
|------|------|-------|-----|------|
| 1 | EtOH | 9 . 6 | — | — |
| 1 | EtOH | 1 9 | — | — |
| 1 | EtOH | 2 9 | — | — |
| 1 | EtOH | 5 0 | — | — |
| 1 | EtOH | 8 9 | — | — |

Example 5 The procedure of an example 5 was repeated using a series of formulations which contained chlorhexidine as a biological activator. Various quantity of a solvent, SAIB, and the formulation containing an additive were prepared.

The formulation by which chlorhexidine was biologically added as activity matter is indicated to the following table 5.

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Although the aforementioned examples of the present invention disclose specific embodiments thereof, it is believed that the substitution of an D-2-alkylTryptophan in bioactive peptide containing at least one Tryptophan residue will yield bioactive peptides providing the advantages and benefits discussed above.

The incorporation of a D-2-alkylTryptophan in bioactive peptides as described above provides a method for prolonging and preserving the activity of such peptides. When analogous bioactive peptides not substituted with an D-2-alkylTryptophan are exposed to various processing conditions and substances, the activity of such peptides may be adversely effected.

Sterilizing procedures used in the pharmaceutical industry may expose bioactive compounds to ionizing radiation. Such radiation may effect the formation of reactive radicals. Tryptophan containing peptides are particularly susceptible to attack by such radicals and such attack may render the peptide ineffective, or possibly toxic. Furthermore, various formulating compounds, such as polylactic-polyglycolic acid polymers may contain active, or activated groups which may also attack Tryptophan containing bioactive peptides. The present invention provides a method for protecting a tryptophan containing bioactive peptide from these manufacturing hazards while also increasing the peptides resistance to oxidative degradation after formulation is complete. It is believed that the presence of the alkyl group at the number 2 position of the Tryptophan increases the stability of the pyrrole ring wherein attack by reactive radicals and active or activated groups occurs.

While it is apparent that the invention herein disclosed is well calculated to fulfill the objects above stated, it will be appreciated that numerous embodiments and modification may be devised by

table 7.

表 7

| %薬剤 | 溶剤 | %溶剤 | 添加剤 | %添加剤 | 溶解度 |
|--------|--------|--------|-----------|------|------------------|
| 2. 6 8 | EtOH | 1 9. 1 | — | — | 不溶性 |
| 2. 4 8 | | 1 5. 6 | — | — | 不溶性 |
| 2. 4 0 | | 9. 6 | — | — | 不溶性 |
| 2. 6 8 | | 7 | — | — | 不溶性 |
| 2. 4 3 | | 7. 1 | スクロース | 2. 6 | 不溶性 |
| 2. 5 6 | | 3. 6 | スクロース | 5. 1 | 不溶性 |
| 2. 3 9 | | 2 8. 7 | C A B | 4. 8 | 可溶性 |
| 2. 4 4 | | 2 8. 6 | PEG (1K) | 4. 8 | 不溶性 |
| 2. 8 9 | | 2 8. 7 | PVP (25) | 4. 8 | 不溶性 |
| 2. 3 8 | | 2 8. 3 | PEG (10K) | 5. 3 | 不溶性 |
| 2. 3 5 | | 3 6. 3 | C A P | 5. 2 | 可溶性 |
| 2. 5 7 | トリアセチン | 5 0 | — | — | 不溶性 |
| 2. 8 9 | | 3 0 | — | — | 不溶性 |
| 2. 4 3 | | 1 1. 5 | — | — | 不溶性 |
| 2. 5 8 | DMSO | 5 0 | — | — | 可溶性 (し かし、褐色) |
| 2. 4 5 | | 3 0. 5 | — | — | 不溶性 |
| 2. 3 6 | | 1 0. 2 | — | — | 不溶性 |

The emission characteristic of the diclofenac in various solvents is shown in drawing 9 -12.

Example 7 The procedure of an example 3 was repeated using a series of formulations which contained the doxycycline as a biological activator. The solvent of various amounts, SAIB, and the formulation containing an additive were prepared.

The formulation which added the doxycycline as activity matter biologically is indicated to the following table 8.

表 8

| %薬剤 | 溶剤 | %溶剤 | 添加剤 | %添加剤 | 溶解度 |
|--------|-------|-----|-----|------|------|
| 5 | EtOH | 1 5 | — | — | 不溶性 |
| 2. 5 6 | | 1 5 | — | — | 不溶性 |
| 4. 9 7 | EtOAc | 3 0 | — | — | 不溶性 |
| 2. 5 | EtLac | 3 0 | — | — | 不溶性 |
| 2. 4 5 | P C | 3 0 | — | — | 不溶性 |
| 2. 5 | G F | 3 0 | — | — | 可溶性 |
| 2. 5 | DMSO | 3 0 | — | — | 一時的に |

In order to promote the fusibility of the doxycycline, few quantity of DMSO was used with the combination of SAIB/EtOH/CAB. These formulations are shown in the following table 9.

表 9

| %ドキシサイクリン | %EtOH | %CAB | %DMSO | 溶解度 |
|-----------|-------|------|-------|--------------------|
| 3.01 | 49 | 6.7 | 7.6 | 可溶性 |
| 4.03 | 47 | 8.9 | 7.9 | 可溶性 |
| 3.07 | 42 | 5.6 | 7.4 | 不溶性 |
| 4.17 | 72 | 21 | 7.5 | 可溶性 (注: SAIBなし) |

Example 8 The procedure of an example 3 was repeated using a series of formulations which contained flurbiprofen as a biological activator. The solvent of various amounts, SAIB, and the formulation containing an additive were prepared.

The formulation which added flurbiprofen as activity matter biologically is indicated to the following table 10.

表 10

| %薬剤 | 溶剤 | %溶剤 | 添加剤 | %添加剤 | 溶解度 |
|------|------|-----|-----|------|-----|
| 2.48 | EtOH | 15 | — | — | 可溶性 |
| 4.98 | EtOH | 15 | — | — | 可溶性 |
| 9.98 | EtOH | 15 | — | — | 可溶性 |
| 4.99 | EtOH | 45 | CAB | 5.0 | 可溶性 |
| 9.92 | EtOH | 45 | CAB | 5.0 | 可溶性 |

The emission characteristic of flurbiprofen is shown in drawing 13.

Example 9 The procedure of an example 3 was repeated using a series of formulations which contained naproxen (free acid) as a biological activator. The solvent of various amounts, SAIB, and the formulation containing an additive were prepared.

The formulation which added naproxen (free acid) as activity matter biologically is indicated to the following table 10.

表 11

| %薬剤 | 溶剤 | %溶剤 | 添加剤 | %添加剤 | 溶解度 |
|-----|----|-----|-----|------|-----|
| 5.2 | GF | 21 | — | — | 可溶性 |
| 3.6 | GF | 37 | — | — | 可溶性 |
| 4.1 | GF | 44 | — | — | 可溶性 |

Example 10 The procedure of an example 3 was repeated using a series of formulations which contained naproxen (sodium salt) as a biological activator. Various quantity of a solvent, SAIB, and the formulation containing an additive were prepared.

Naproxen (sodium salt) cannot be dissolved in EtOH and EtOAc. The formulation which added naproxen (sodium salt) as activity matter biologically is indicated to the following table 12.

表 1 2

| %薬剂 | 溶剂 | %溶剂 | 添加剂 | %添加剂 | 溶解度 |
|-------|-----|-----|-----|------|-----|
| 5 . 2 | G F | 2 1 | — | — | 不溶性 |
| 3 . 4 | G F | 3 7 | — | — | 可溶性 |
| 3 . 9 | G F | 4 4 | — | — | 可溶性 |

The emission characteristic of the naproxen (a free acid and sodium salt) in various solvents is shown in drawing 14.

Example 11 The procedure of an example 3 was repeated using a series of formulations which contained naproxen (sodium salt) and naproxen (free acid) as a biological activator. The solvent of various amounts, SAIB, and the formulation containing an additive were prepared.

The formulation which added naproxen (sodium salt) and naproxen (free acid) as activity matter biologically is indicated to the following table 13.

表 1 3

| %遊離酸 | %ナトリウム塩 | 溶剂 | %溶剂 | 溶解度 |
|---------|---------|-------|-----|-----|
| 2 . 3 8 | 2 . 5 5 | P C | 2 0 | 不溶性 |
| 1 . 2 8 | 3 . 5 6 | G F | 2 0 | 不溶性 |
| 2 . 2 7 | 2 . 7 8 | EtLac | 3 0 | 可溶性 |
| 2 . 4 9 | 2 . 5 5 | G F | 2 0 | 可溶性 |

Example 12 The procedure of an example 3 was repeated using a series of formulations which contained theophylline as a biological activator. Various quantity of a solvent, SAIB, and the formulation containing an additive were prepared.

The formulation by which theophylline was biologically added as activity matter is indicated in the following table 14.

表 1 4

| %薬剂 | 溶剂 | %溶剂 | 添加剂 | %添加剂 | 溶解度 |
|------|---------------------|------|-------|------|-----|
| 0. 5 | EtOH | 1 5 | — | — | 不溶性 |
| 1 | EtOH | 1 5 | — | — | 不溶性 |
| 2. 5 | EtOH | 1 5 | — | — | 不溶性 |
| 5 | EtOH | 1 5 | — | — | 不溶性 |
| 1 0 | EtOH | 1 5 | C A B | 5 | 不溶性 |
| 2. 5 | EtOH | 5 3 | C A B | 1 0 | 不溶性 |
| 2. 5 | EtOH | 4 7 | C A B | 1 5 | 不溶性 |
| 2. 5 | EtOH | 4 3 | C A P | 5 | 不溶性 |
| 2. 5 | EtOH | 5 3 | C A P | 1 0 | 不溶性 |
| 2. 6 | EtOH | 4 8 | C A P | 1 5 | 不溶性 |
| 2. 5 | EtOH | 4 3 | — | — | 不溶性 |
| 5. 2 | EtOAc | 4 8 | — | — | 不溶性 |
| 4. 8 | EtOAc | 2 9 | — | — | 不溶性 |
| 5. 0 | EtOAc | 9. 5 | — | — | 不溶性 |
| 5. 0 | FCH ₂ OH | 4 8 | — | — | 不溶性 |
| 5. 2 | FCH ₂ OH | 2 9 | — | — | 不溶性 |
| 5. 0 | FCH ₂ OH | 1 1 | — | — | 不溶性 |
| 5. 4 | EtOH | 1 0 | — | — | 不溶性 |
| 6. 5 | EtOH | 2 0 | — | — | 不溶性 |
| 5. 5 | EtOH | 3 0 | — | — | 不溶性 |
| 5. 5 | EtOH | 2 5 | C A B | 5. 5 | 不溶性 |
| 7. 2 | EtOH | 3 4 | C A B | 5. 4 | 不溶性 |
| 5. 4 | EtOH | 4 5 | C A B | 5. 9 | 不溶性 |
| 5. 1 | P C | 1 1 | — | — | 不溶性 |
| 5. 5 | P C | 2 0 | — | — | 不溶性 |
| 5. 5 | P C | 3 1 | — | — | 不溶性 |

The emission characteristic of the theophylline in propylene carbonate is shown in drawing 16. Although the emission characteristic was tried in the formulation of the following containing theophylline, the sample became muddy considerably.

The amount of the ingredient in these formulations is indicated to the following table 15.

表 1 5

| %薬剂 | 溶剂 | %溶剂 | 添加剂 | %添加剂 | 溶解度 |
|-----|------|-----|-----------|------|-----|
| 4.9 | EtOH | 1.6 | PVP (K25) | 5.1 | 不溶性 |
| 5.0 | EtOH | 4.0 | PVP (K25) | 5.0 | 不溶性 |
| 5.1 | EtOH | 1.5 | PEG (1K) | 5.0 | 不溶性 |
| 5.0 | EtOH | 4.0 | PEG (1K) | 5.0 | 不溶性 |
| 4.9 | EtOH | 4.0 | PEG (10K) | 5.4 | 不溶性 |
| 4.9 | EtOH | 1.6 | PEG (10K) | 4.9 | 不溶性 |

Example 13 The formulation was prepared by 80% of SAIB, and 15% of ethanol, and filled up the aerosol can with the obtained solution. This solution was sprayed on the agar plate and the continuous film which has adhesive there was formed.

Example 14 A series of formulations were prepared by 80% of SAIB, and 0.02% of methylene blue, and the ratio of ethanol and CAB was changed in 1:0-1:1. This formulation was sprayed on gelatin. Dilution of the methylene blue to gelatin was controlled by making the content of CAB increase.

Example 15 SAIB was heated to 60-degreeC. The formulation was separately produced by 1%, 2%, 5%, and 10% of tetracycline. The syringe equipped with the needle of 21 gages was filled up with this formulation. The formulation was extruded to the butter of 37-degreeC with the syringe by manual operation. At the temperature of about 43-degreeC, the formulation was able to be extruded easily.

Example 16 Preparation and the property of a gargle A polyoxyethylene (7.680g, 20E.C.) almond oil (Crovol A-70), 4.042g deca glycerol tetra-oleate (Caprol IOG40), and a 11.721g middle chain triglyceride (Neobee M-5) were mixed with the suitable mixed container (it is the kettle of the surface sweep mold of a single acting type with a jacket). This mixture was heated to about 65-degreeC. It became the organic phase which mixed and heated the methylparaben (0.500g), 0.250g propylparaben, 0.125g cetyl pyridinium chloride, a 0.125g benzoic acid, and 0.625g cane-sugar acetic-acid isobutyric-acid ester. The mixture of this organic phase was maintained to about 65-degreeC through the attached component. Zinc guru KONETO (zinc gluconate) (0.250g), the 0.125g sodium benzoate, the acid that cannot go away 0.0625g, and the 12.5g sorbitol were dissolved in 221.10g deionized water. The mixture of the phase of this water was heated to about 65-degreeC. both the mixture of an organic phase, and the mixture of the aqueous phase -- although -- after reaching the temperature, the aqueous phase was added, stirring to an oil phase slowly. When the aqueous phase had been completely added to the oil phase, two drops of green food coloring agents and a 1.000g pepper mint oil were added, and it was often stirred, and was made the formulation. And to the room temperature, it cooled quickly and packaging of this mixture was carried out. The decrement of the water under processing in this scale was about 10.1g.

The final product was what has the following presentations.

表 1 6

| うがい薬成分 | 濃度 (w t.) % |
|--------------------|-------------|
| PEG-20アーモンド油 | 3. 0 7 |
| 中間鎖トリグリセリド | 4. 7 0 |
| デカグリセロールテトラオレート | 1. 6 2 |
| 水 | 8 4. 4 |
| トリス(ヒドロキシメチル)アミン | 0. 2 5 0 |
| ペパーミント油 | 0. 4 0 0 |
| メチルパラベン | 0. 2 0 0 |
| プロピルパラベン | 0. 1 0 0 |
| セチルトリメチルアンモニウムクロリド | 0. 0 5 0 |
| 亜鉛グルコネート | 0. 1 0 0 |
| サッカリン | 0. 0 2 0 |
| ソルビトール | 5. 0 0 |
| 安息香酸ナトリウム | 0. 0 5 0 |
| クエン酸 | 0. 0 2 5 |
| 安息香酸 | 0. 0 5 0 |
| 緑の食品着色剤 | 適宜 |

Example 17 The piece of a vascular transplant (vascular graft) was immersed in 61.8% of SAIB, 10.0% of CAB, and the solution that consists of 28.2% of ETOH, and 1% of heparin was added in this solution. The solution was drained from this transplant and physiological sodium chloride solution washed. The piece of a vascular transplant was transplanted to the dog. After transplanting, even if compared with the piece of a control vascular transplant, there was no blood coagulation in the inner surface of a transplant.

Example 18 5% of CAB, 45% of ethanol, and the formulation that consists of 50% of SAIB were prepared. The phenol which is in these in the transformer homing growth factor beta of 0.05 - 0.0005% of amount or 1 - 5.1% of range was added. Pouring this compound into the inguinal canal of a dog, the compound pulled out the cell reaction which results in inguinal canal lock out there.

Example 19 10% of CAB, 45% of ethanol, and the compound that consists of 45% of SAIB were sprayed on the uterine horn of a rabbit which exfoliated surgically. Although adhesion with all these surgical fields was not shown at the time of reexamination, it was that which is biologically tolerant fully about those each.

Example 20 Drawing 17 is a graph which shows the burst size of two formulations. One formulation (pinstripes)

The remainder is diH₂O including **, 3.2% of SAIB, 15.1% of ETOH, and 0.00395% of methylene blue. Another formulations (slanting stripes) were 0% of SAIB, 28.9% of ETOH, 0.00395% of methylene blue, and diH₂O.

The 1 inch split which consists of a natural collagen is excised, and it is PBS (pH6.8).

It came out and washed, and for 9 minutes was immersed in the formulation, it put into the washed test tube and PBS was filled. At some times, PBS was decanted, UV analysis was carried out, and it added to the test tube with which new PBS contained the collagen. Please refer to drawing 17.

Deformation and modification of the compound and approach which were used at this invention, i.e., here, are easy for this contractor by above-mentioned detailed explanation. Such deformation and modification are included in an attached claim, and become things.

[Translation done.]

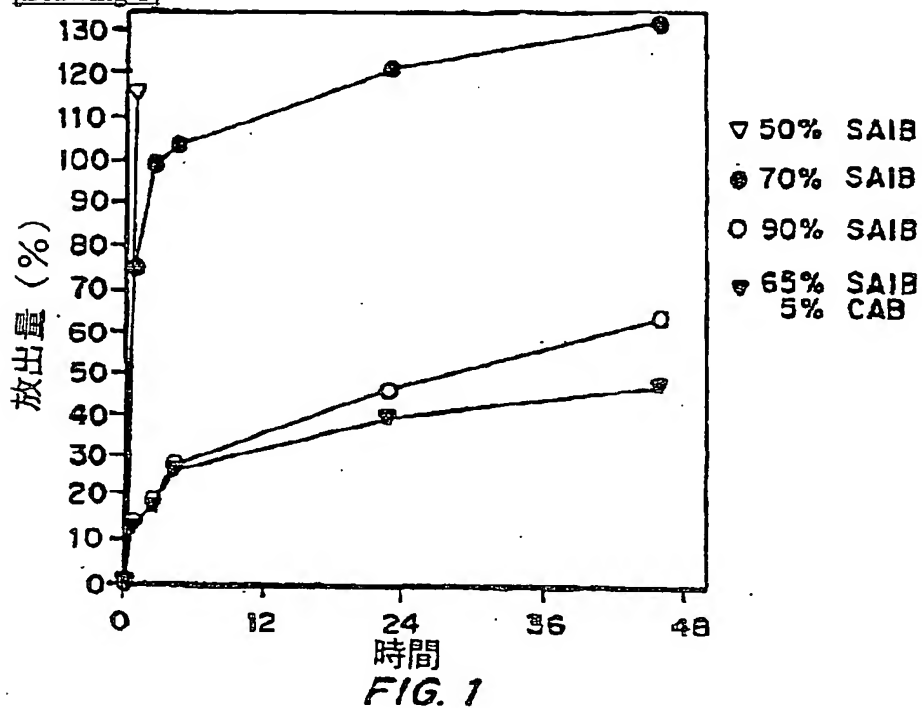
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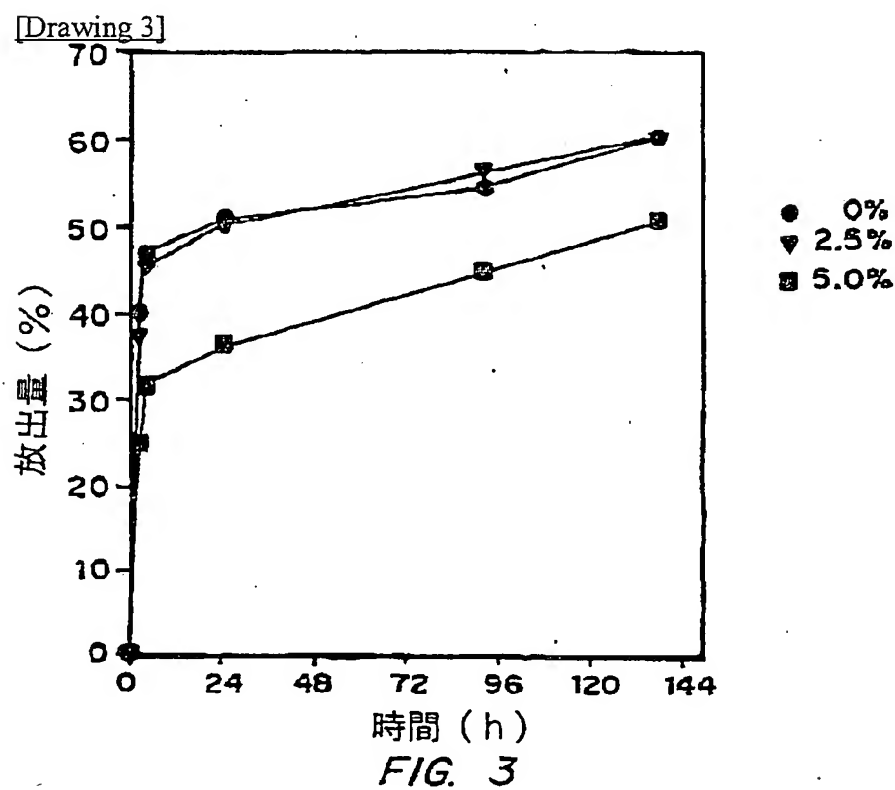
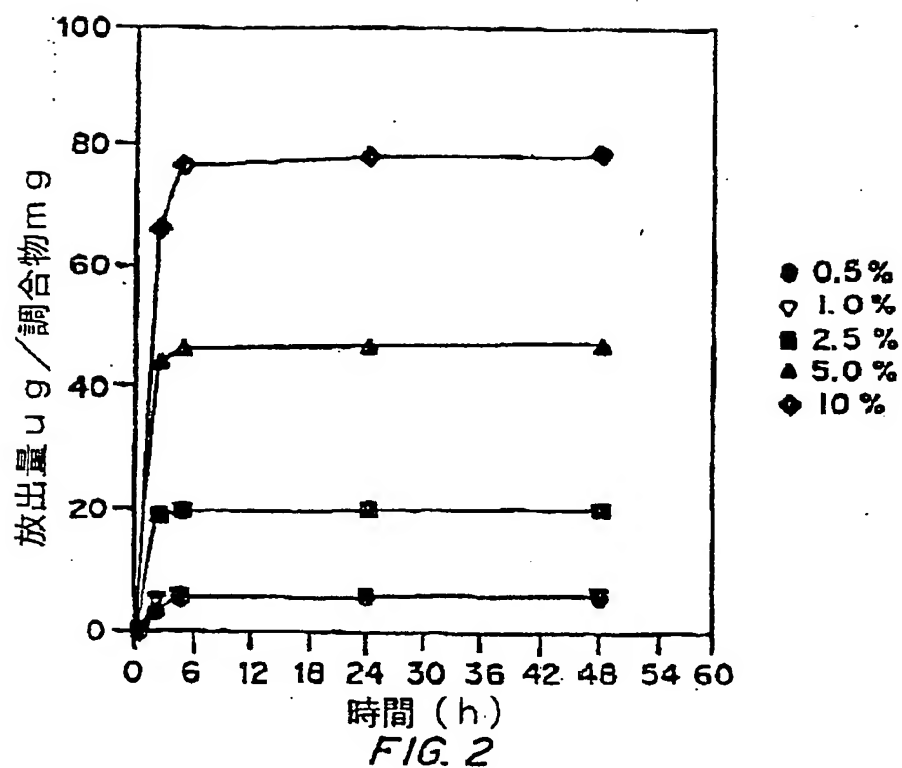
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DRAWINGS

[Drawing 1]



[Drawing 2]



[Drawing 4]

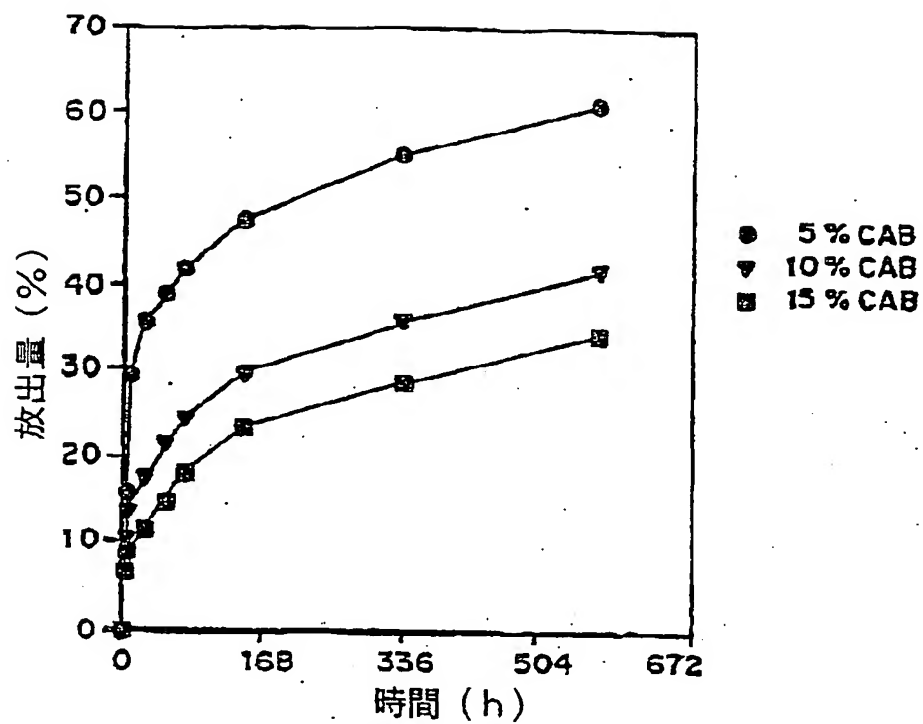


FIG. 4

[Drawing 5]

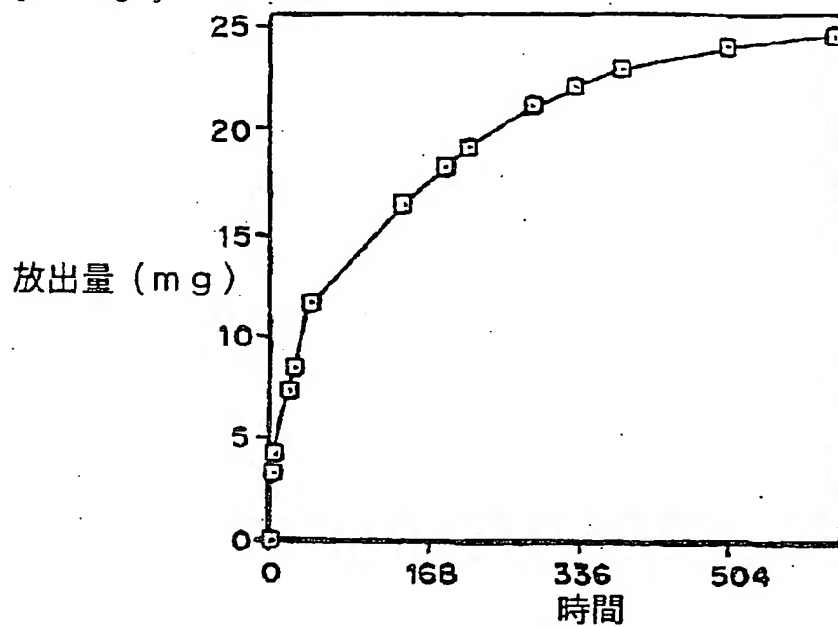
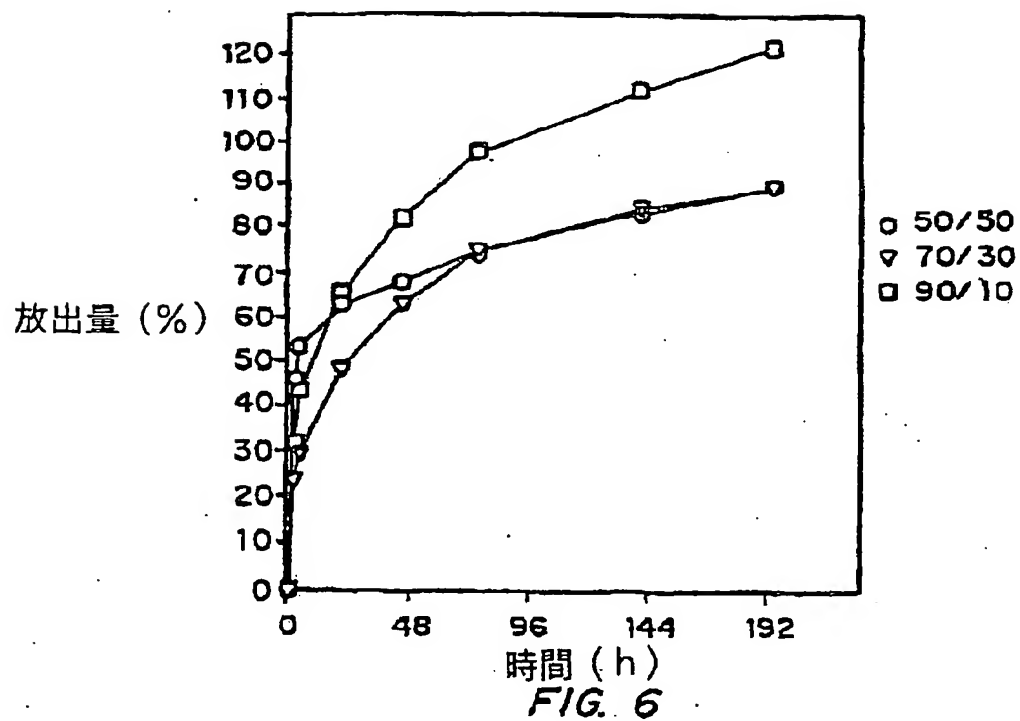
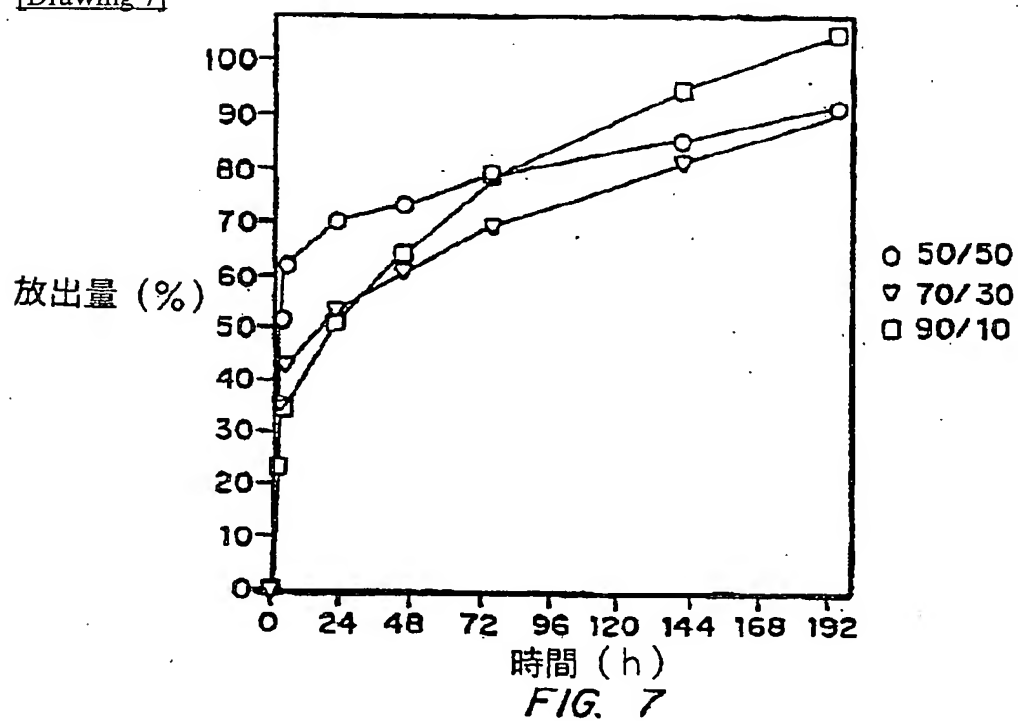


FIG. 5

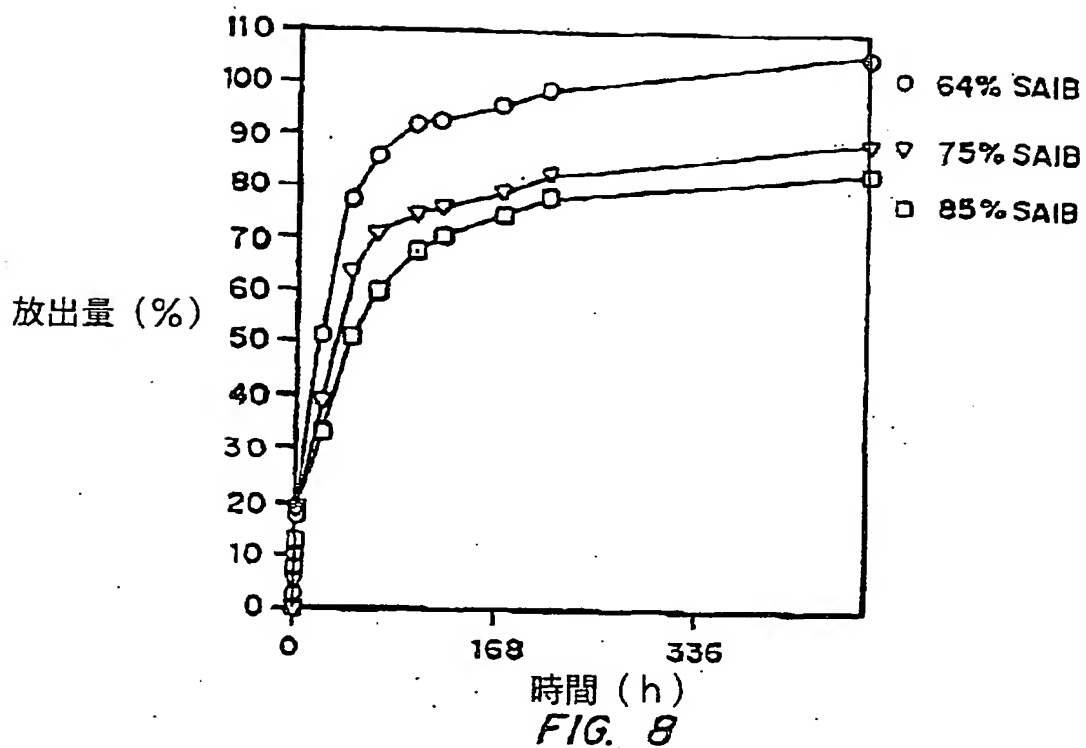
[Drawing 6]



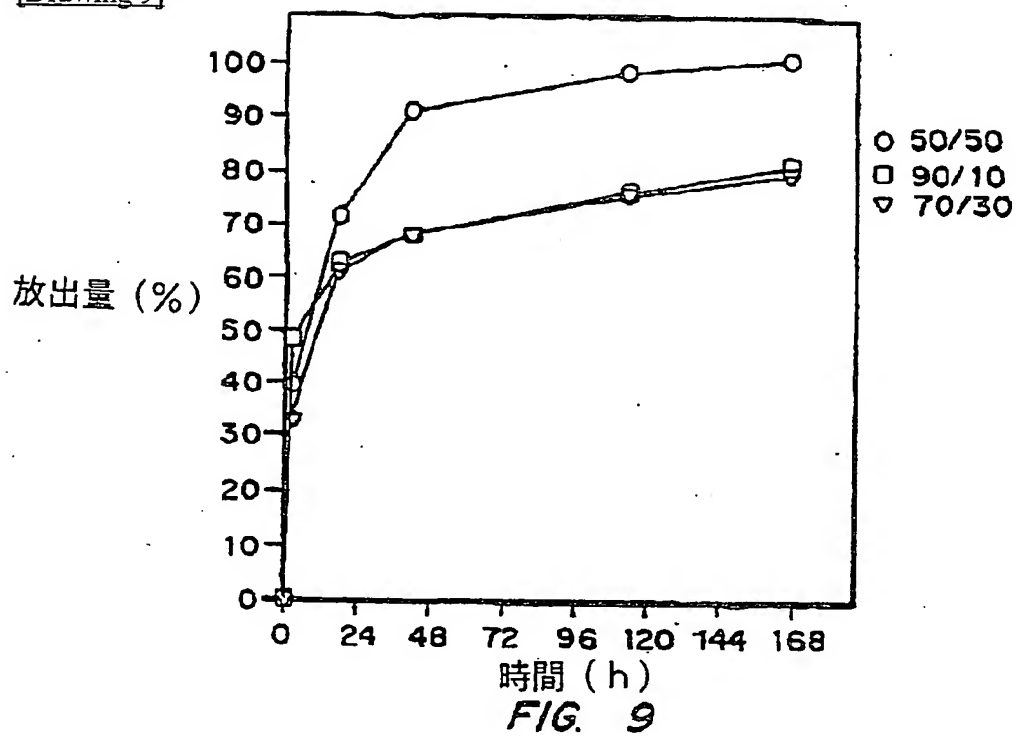
[Drawing 7]



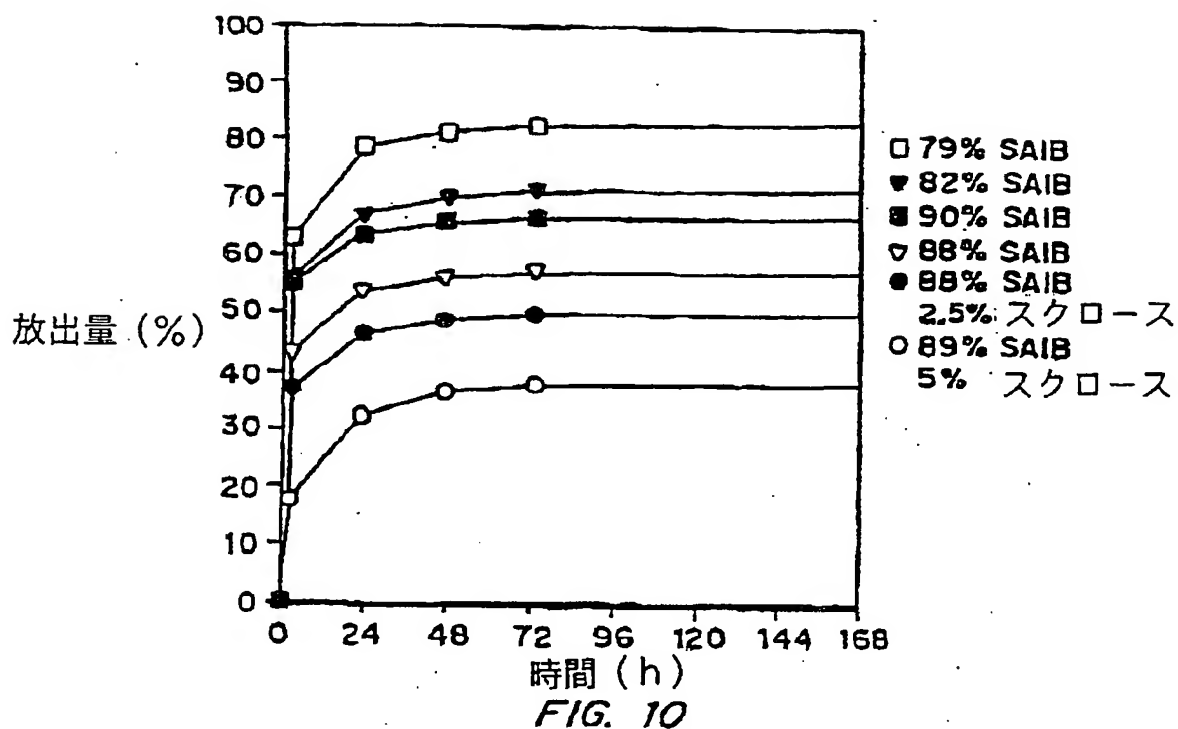
[Drawing 8]



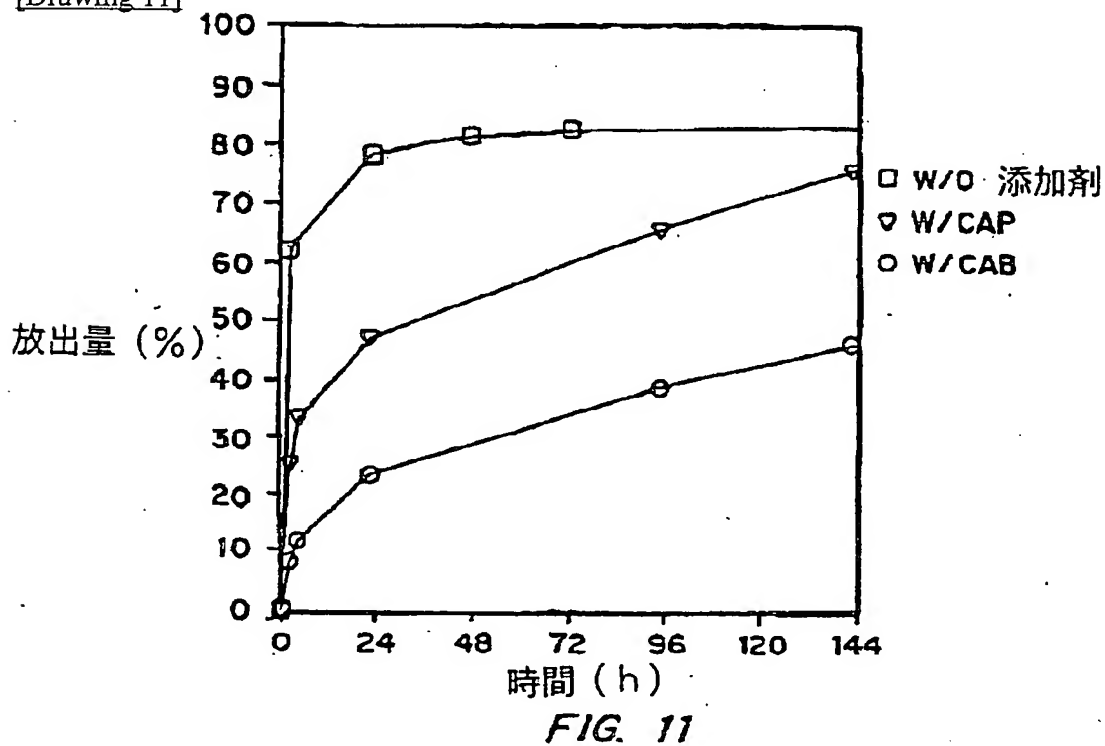
[Drawing 9]



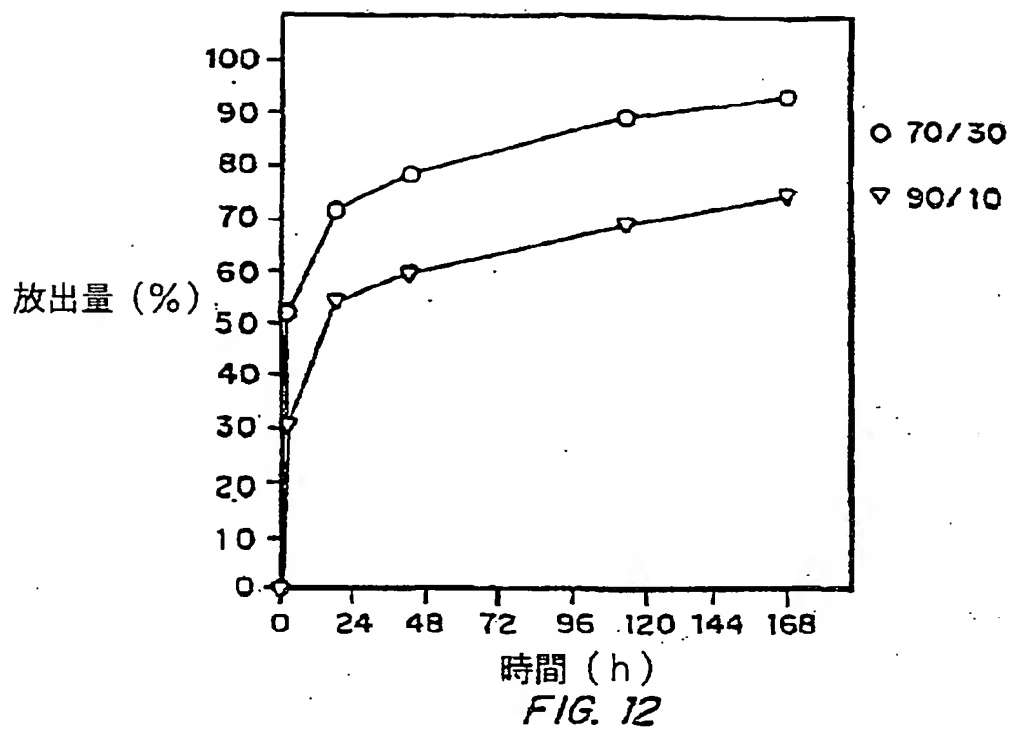
[Drawing 10]



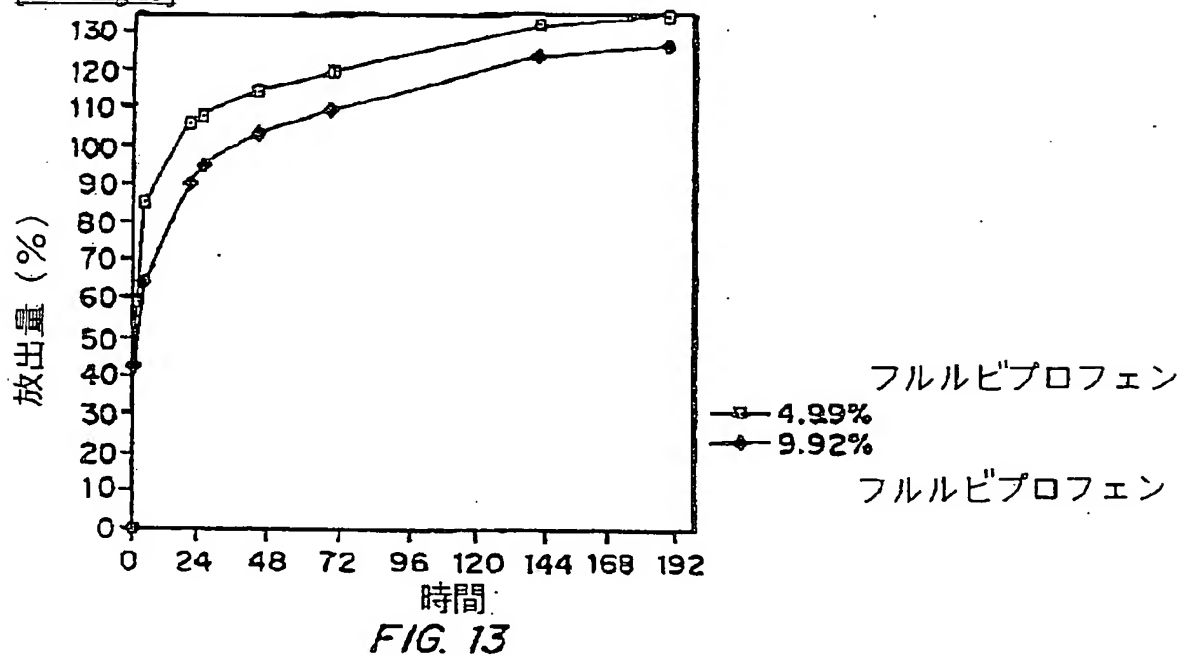
[Drawing 11]



[Drawing 12]



[Drawing 13]



[Drawing 14]

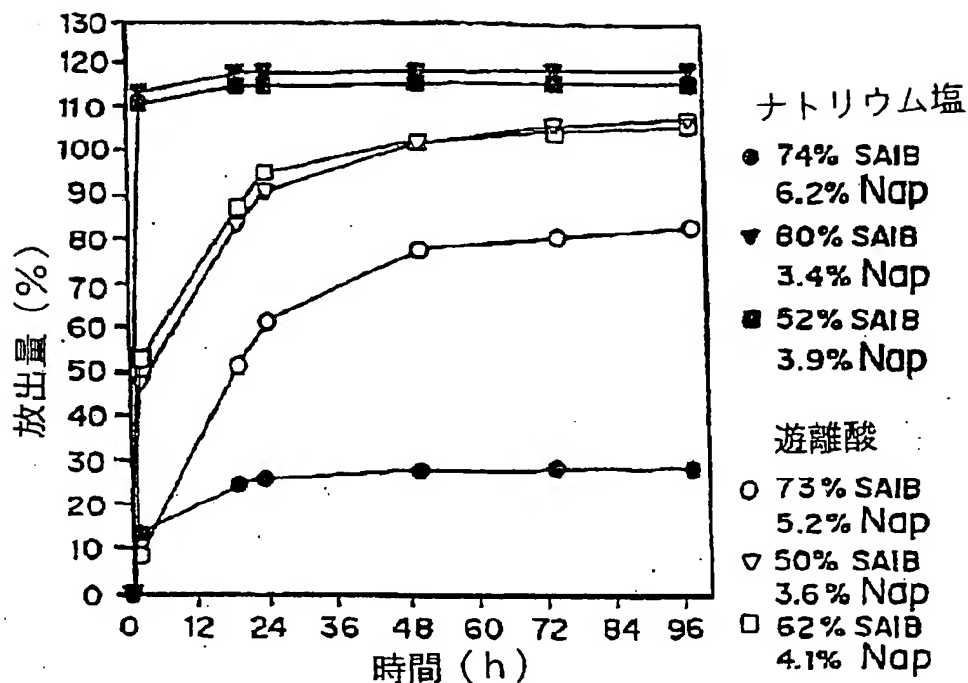


FIG. 14

[Drawing 15]

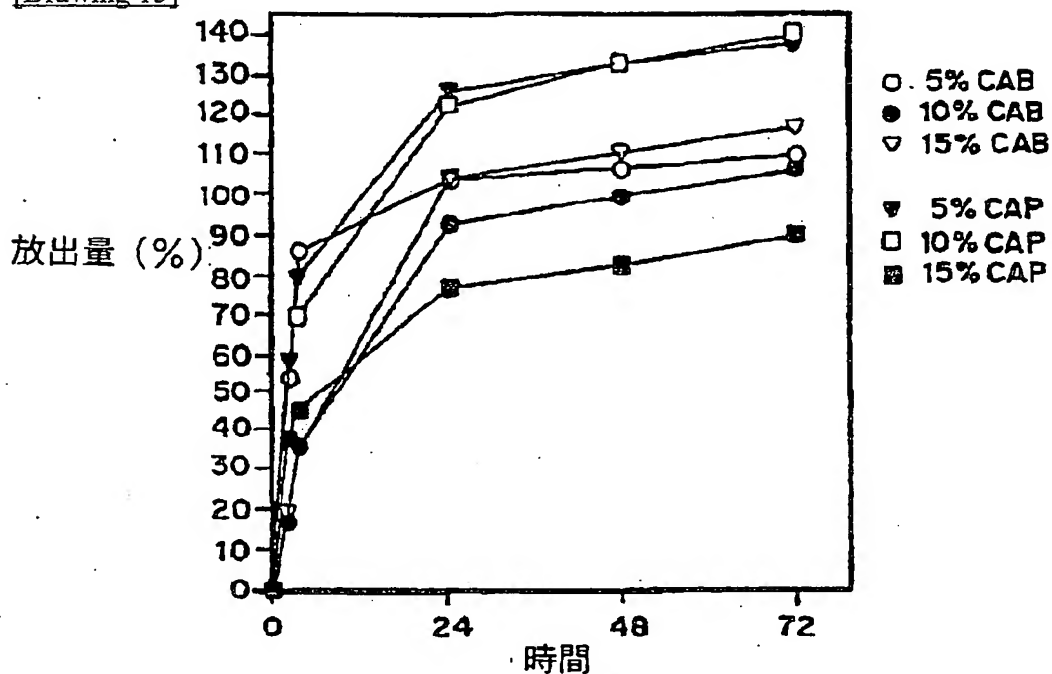


FIG. 15

[Drawing 16]

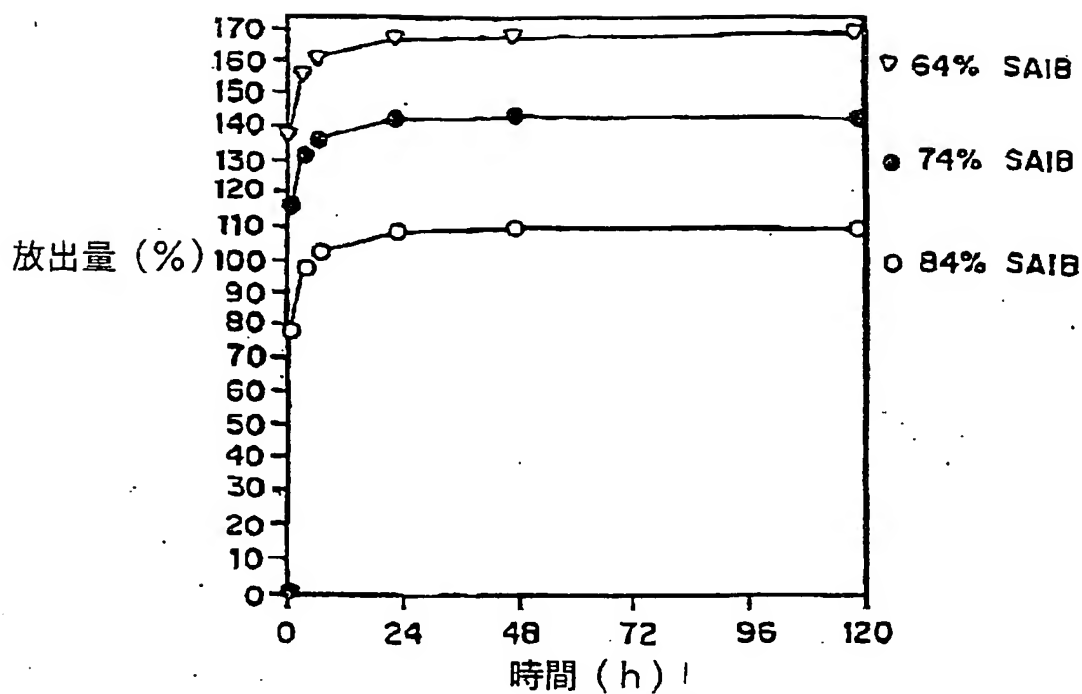


FIG. 16

[Drawing 17]

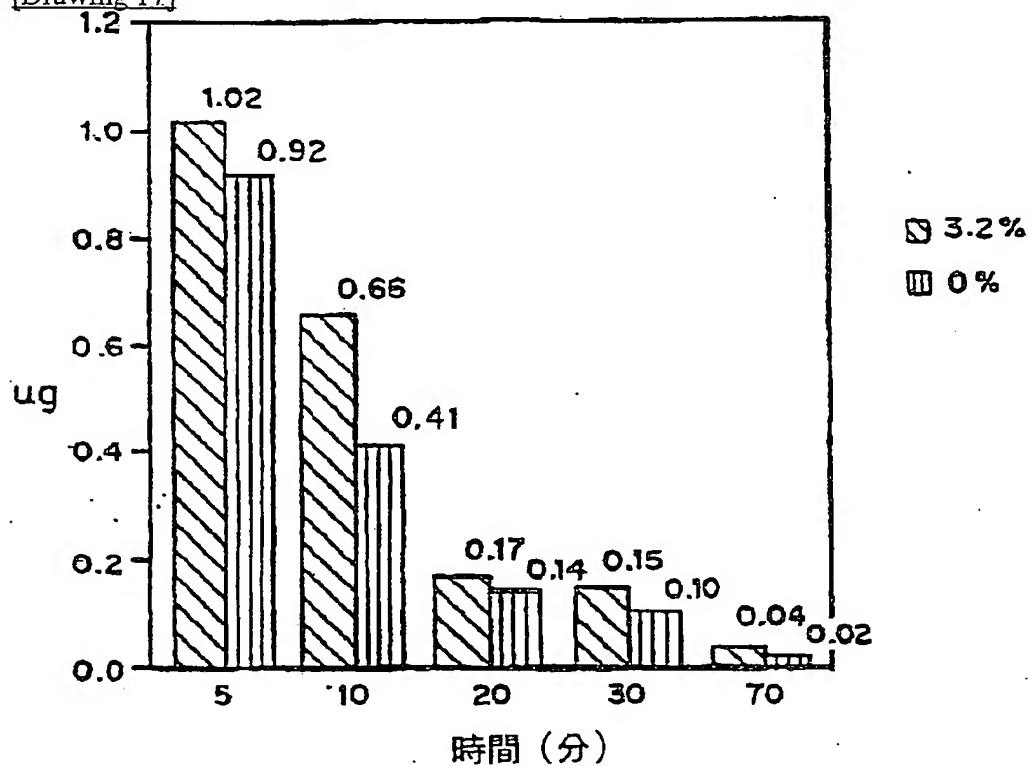


FIG. 17

[Translation done.]

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CORRECTION OR AMENDMENT

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手続補正書

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特許庁長官 殿

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4. 補正対象書類名

明細書

5. 補正対象項目名

特許請求の範囲

6. 補正の内容

別紙の通り

【特許請求の範囲】

1. 生体活性物質の送達のための液状配合物であって、
 - (a) 周囲条件または生理学的条件下において純粋には結晶化しない、37℃にて少なくとも5000 cPの粘度を有する、非重合性の、非水溶性の高粘性液状キャリア材料と、
 - (b) 生体活性物質を含む液状配合物。
2. 非重合性で非水溶性の高粘性液状キャリア材料が、しょう糖酢酸イソ酪酸エステルである請求項1に記載の配合物。
3. 非重合性で非水溶性の高粘性液状キャリア材料が、配合物の全重量に対して約9.5重量%～約10重量%の量で存在する請求項2に記載の配合物。
4. 非重合性で非水溶性の高粘性液状キャリア材料が、配合物の全重量に対して約9.5重量%～約2.5重量%の量で存在する請求項3に記載の配合物。
5. 非重合性で非水溶性の高粘性液状キャリア材料が、配合物の全重量に対して約8.5重量%～約4.5重量%の量で存在する請求項3に記載の配合物。
6. 非重合性で非水溶性の高粘性液状キャリア材料が溶解する溶媒を含む請求項2に記載の配合物。
7. 溶媒が、エタノール、ジメチルスルホキシド、エチルラクテート、エチルアセテート、ベンジルアルコール、トリアセチン、2-ピロリドン、N-メチルピロリドン、プロピレンカーボネート及びグリコフロールからなる群から選ばれた溶媒である請求項6に記載の配合物。
8. 溶媒が、配合物の重量に対して約10重量%～約50重量%の量で存在する請求項6に記載の配合物。
9. 配合物がさらに添加剤を含む請求項2に記載の配合物。
10. 添加剤が、配合物の全重量に対して約1重量%～約20重量%の量で存在する請求項9に記載の配合物。
11. 添加剤が、生分解性ポリマー、非生分解性ポリマー、天然油、

合成油、炭水化物、無機塩及び不活性有機化合物からなる群から選ばれた請求項 9 に記載の配合物。

12. 添加剤が、ポリ(ラクチド)、ポリ(ラクチド-コ-グリコリド)、ポリ(グリコリド)、ポリ(カプロラクトン)、ポリ(D,L-乳酸)、ポリビニルピロリドン、ポリエチレングリコール、酸化セルロース、酢酸セルロース、酢酸プロピオン酸セルロース、ピーナツ油、ごま油及びしじみ糖からなる群から選ばれた請求項 9 に記載の配合物。

13. 局所的投与に適した請求項 2 に記載の配合物。

14. 体系的投与に適した請求項 2 に記載の配合物。

15. 経口的投与に適した請求項 2 に記載の配合物。

16. さらに、低粘性液状キャリア材料を含んだ請求項 2 に記載の配合物。

17. 低粘性液状キャリア材料が 1000 cP より小さい粘度を有する請求項 16 に記載の配合物。

18. 生体活性物質が、農業目的に有用である請求項 2 に記載の配合物。

19. 生体活性物質が、人の治療目的に有用である請求項 2 に記載の配合物。

20. 生体活性物質が、獣医学的目的に有用である請求項 2 に記載の配合物。

21. 生体活性物質が、雑草の駆除に有用である請求項 18 に記載の配合物。

22. 生体活性物質が、昆虫の駆除に有用である請求項 18 に記載の配合物。

23. 配合物が、害虫の駆除に有用である請求項 18 に記載の配合物。

24. 生体活性物質がステロイドである請求項 19 に記載の配合物。

25. 配合物が、シラミ駆除に有用である請求項 2 に記載の配合物。

26. 配合物が、ふけ防止に有用である請求項 2 に記載の配合物。

27. 生体活性物質が、ペプチド、タンパク質、核タンパク質、ムコ

タンパク質、リボタンパク質及び合成ポリペプチドからなる群から選ばれた請求項 2 に記載の配合物。

28. 生体活性物質が、テオフィリン、フルルビプロフニン、ナプロキセン、クロルヘキシジン、ジクロフェナク、エストロゲン、プロゲステロン、テトラサイクリン、アジスロマイシン、デキサメタゾン、17- β -エストラジオール、ドキシサイクリン、ヘパリン、核酸、ヌクレオチド、ヌクレオシド及びオリゴヌクレオチドからなる群から選ばれた請求項 2 に記載の配合物。

29. 生体活性物質が、プロゲステロンとニストラジオールの組み合わせである請求項 2 に記載の配合物

30. 生体活性物質が、薬剤である請求項 2 に記載の配合物。

31. 生体活性物質が、ワクチン、麻酔薬、ホルモン、抗生物質、抗精神薬、ステロイド及び化学療法薬剤からなる群から選ばれた請求項 2 に記載の配合物。

32. 生体活性物質が、抗ウイルス薬である請求項 1 に記載の配合物。

33. 生体活性物質が、成長因子である請求項 2 に記載の配合物。

34. 生体活性物質が、トランスフォーミング成長因子- β である請求項 2 に記載の配合物。

35. 生体活性物質が、遺伝子である請求項 2 に記載の配合物。

36. 生体活性物質が、脂質である請求項 2 に記載の配合物。

37. 生体活性物質が、ビタミンである請求項 2 に記載の配合物。

38. 直腸投与に適した請求項 2 に記載の配合物。

39. 経投与に適した請求項 2 に記載の配合物。

40. 鼻腔投与に適した請求項 2 に記載の配合物。

41. 経口投与に適した請求項 2 に記載の配合物。

42. 外科的癒着の阻止に適した請求項 1 に記載の配合物。

43. 骨組み、間隙充填、または組織再生に適した請求項 1 に記載の配合物。

44. 腫れへの血液供給を阻止するために用いるための請求項 1 に記

載の配合物。

45. 組織接着剤に適した請求項2に記載の配合物。

46. 傷の治療に適した請求項2に記載の配合物。

47. 非重合性で非水溶性の高粘性液状キャリア材料が、二糖エステルである請求項1に記載の配合物。

48. 請求項1に記載の配合物であって、

(a) 封入されたマイクロスフェアを与えるために、生体活性物質をマイクロスフェア内に封入する工程と

(b) 所望の配合物を与えるために、封入されたマイクロスフェアをキャリア材料と混合する工程とを含むことにより生体活性物質が調整される配合物。

49. 生体活性物質が、シクロデキストリンのような錯化剤と錯体を形成することができる請求項1に記載の配合物。

50. 生体活性物質が、プロドラッグの形態である請求項1に記載の配合物。

51. 配合物が経口投与のためのゼラチンカプセル内に配置される請求項1に記載の配合物。

52. 配合物がマイクロスフェアまたはマイクロカプセル内に封入される請求項1に記載の配合物。

53. マイクロスフェアが、生分解性ポリマーである請求項52に記載の配合物。

54. 配合物が、不活性の薬学的な賦形剤と会合させられ、該賦形剤が随意に、スフェアあるいはその他の形状に加工されて、投薬形態の中に組み込むことができる請求項1に記載の配合物。

55. 請求項1に記載の配合物を投与する方法であって、

(a) 所定量の配合物を供給する工程と、

(b) 配合物をホストにエマルジョンまたは溶液で投与する工程とを含む方法。

56. 配合物をホストに注射で投与する工程を含む請求項1に記載の

配合物を投与する方法。

57. 医療用または外科用インプラント、フィルム若しくはグラフトの配合物であって、

周囲条件または生理学的条件下において純粋には結晶化しない、37℃にて少なくとも5000cPの粘度を有する非重合性で非水溶性の高粘性液状キャリア材料を含む配合物。

58. 非重合性で非水溶性の高粘性液状キャリア材料が、ヒyaluronateイソ酸エステルである請求項57に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

59. 非重合性で非水溶性の高粘性液状キャリア材料が、37℃にて少なくとも10000cPの粘度を有する請求項57に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

60. 非重合性で非水溶性の高粘性液状キャリア材料が、37℃にて少なくとも15000cPの粘度を有する請求項59に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

61. 非重合性で非水溶性の高粘性液状キャリア材料が、37℃にて少なくとも20000cPの粘度を有する請求項60に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

62. 非重合性で非水溶性の高粘性液状キャリア材料が、37℃にて少なくとも25000cPの粘度を有する請求項61に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

63. 非重合性で非水溶性の高粘性液状キャリア材料が、37℃にて少なくとも50000cPの粘度を有する請求項62に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

64. 非重合性で非水溶性の高粘性液状キャリア材料が、さらに添加剤を含む請求項57に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

65. 添加剤が、生分解性ポリマー、非生分解性ポリマー、天然油、合成油、炭水化物、炭水化物誘導体、無機塩及び不活性有機化合物か

らなる群から選ばれる請求項 6 4 に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

6 6. 配合物がさらに、制御された放出のための生体活性物質を含む請求項 5 7 に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

6 7. 外科的癒着を阻止する請求項 5 7 に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

6 8. 生体組織の空隙を充填する請求項 5 7 に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

6 9. 組織再生を誘導する請求項 5 7 に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

7 0. 止血剤である請求項 5 7 に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

7 1. 組織接着剤である請求項 5 7 に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

7 2. 生体組織のスカルフオルディングである請求項 5 7 に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

7 3. 創傷の手当材である請求項 5 7 に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

7 4. 非重合性で非水溶性の高粘性液状キャリア材料が、配合物の全重量に対して約 9 9 . 5 重量%～約 1 0 重量%の量で存在する請求項 5 8 に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

7 5. 非重合性で非水溶性の高粘性液状キャリア材料が、配合物の全重量に対して約 9 9 . 5 重量%～約 2 . 5 重量%の量で存在する請求項 5 8 に記載の医療用または外科用インプラント、フィルム若しくはグラフトの配合物。

7 6. 医療的または外科的に移植可能若しくは噴霧可能な配合物である。

(a) 周囲条件または生理学的条件下において純粋には結晶化しない、37℃にて少なくとも5000 cPの粘度を有する、非重合性で非水溶性の高粘性液状キャリア材料と、

(b) 非重合性で非水溶性の高粘性液状キャリア材料が溶解する溶媒との混合物を含む配合物であって、該混合物が37℃で約1000 cPより小さい低粘度を有する配合物。

7.7. 溶媒が、エタノール、ジメチルスルホキシド、乳酸ニチル、酢酸エチル、ベンジルアルコール、トリアセチン、2-ピコリドン、N-メチルピロリドン、プロピレンカーボネート及びグリコノロールからなる群から選ばれる請求項7.6に記載の医療的または外科的に移植可能若しくは噴霧可能な配合物。

7.8. 非重合性で非水溶性の高粘性液状キャリア材料が溶解する溶媒が、移植可能または噴霧可能な配合物の重量に対して約10重量%～約50重量%の量で存在する請求項7.6に記載の医療的または外科的に移植可能若しくは噴霧可能な配合物。

7.9. 必要に応じて、患者のインゴボでインプラント、フィルムまたはグラフトを形成する方法であって、

(1) (a) 周囲条件または生理学的条件下において純粋には結晶化しない、37℃にて少なくとも5000 cPの粘度を有する、非重合性で非水溶性の高粘性液状キャリア材料、及び(b) 非重合性で非水溶性の高粘性液状キャリア材料が溶解する溶媒とを含む混合物であり、該混合物が37℃で約1000 cPより小さい低粘度を有し、該混合物を患者の組織に接触させる方法と、

(2) 溶媒を患者の組織内で消散あるいは拡散させて、それにより非重合性で非水溶性の高粘性液状キャリア材料のインプラント、フィルムまたはグラフトを形成する方法とを含む形成方法。

8.0. 上記接触方法が、上記混合物で血管グラフトをコーティングする方法と、患者に該血管グラフトを移植する方法とを含む請求項7.9に記載の形成方法。

8 1 . 上記接触方法が、上記混合物を患者の組織の管または腔に注入する方法を含む請求項 7 9 に記載の形成方法。

8 2 . 上記接触方法が、上記混合物を患者の組織上に噴霧する方法を含む請求項 7 9 に記載の形成方法。

8 3 . 上記接触方法が、上記混合物からなるペーストを患者の組織上で広げる方法を含む請求項 7 9 に記載の形成方法。

[Translation done.]